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(54) Title: NEW NUCLEOTIDE SEQUENCES

(57) Abstract

The present invention relates to a nucleic acid molecule encoding a GABAB receptor, or a functionally equivalent modified form thereof, said receptor being selected from the group consisting of human and canine GABAB receptors.

NEW NUCLEOTIDE SEQUENCES

TECHNICAL FIELD

5   The present invention relates in particular to nucleic acid molecules encoding $GABA_B$

receptors, and to methods for screening for compounds which are inhibitors of transient

lower esophageal sphincter relaxations (TLESR), said methods comprising the use of a

nucleic acid molecule encoding a $GABA_B$ receptor.

10

BACKGROUND ART

$GABA_B$ receptors

15   GABA (4-aminobutanoic acid) is an endogenous neurotransmitter in the central and

peripheral nervous systems. Receptors for GABA have traditionally been divided into

$GABA_A$ and $GABA_B$ receptor subtypes. $GABA_B$ receptors (for a review see Kerr, D.I.B.

and Ong, J. (1995) Pharmac. Ther. vol. 67, pp.187-246) belong to the superfamily of G-

protein coupled receptors. $GABA_B$ receptor agonists are described as being of use in the

20   treatment of CNS disorders, such as muscle relaxation in spinal spasticity, cardiovascular

disorders, asthma, gut motility disorders such as irritable bowel syndrome and as prokinetic

and anti-tussive agents. $GABA_B$ receptor agonists have also been disclosed as useful in the

treatment of emesis (WO 96/11680).

25   The cloning of the rat $GABA_B$ receptors $GABA_BR1a$ (SEQ ID NOS: 44 and 45) and

$GABA_BR1b$ (SEQ ID NOS: 46 and 47) is disclosed by Kaupmann et al. (1997) Nature,

vol. 386, 239-246. The mature rat $GABA_BR1b$ differed from $GABA_BR1a$ in that the N-

terminal 147 residues were replaced by 18 different residues. It was presumed that the rat

$GABA_BR1a$ and -b receptor variants are derived from the same gene by alternative

30   splicing.

The cloning of the human GABA$_B$ receptor GABA$_B$R1b is disclosed in WO 97/46675.

Reflux

5   In some humans, the lower esophageal sphincter (LES) is prone to relaxing more frequently than in other humans. As a consequence, fluid from the stomach can pass into the esophagus since the mechanical barrier is temporarily lost at such times, an event hereinafter referred to as "reflux".

10   Gastro-esophageal reflux disease (GERD) is the most prevalent upper gastrointestinal tract disease. Current therapy has aimed at reducing gastric acid secretion, or by reducing esophageal acid exposure by enhancing esophageal clearance, lower esophageal sphincter tone and gastric emptying. The major mechanism behind reflux has been considered to depend on a hypotonic lower esophageal sphincter. However, recent research (e.g.

15   Holloway & Dent (1990) Gastroenterol. Clin. N. Amer. 19, 517-535) has shown that most reflux episodes occur during transient lower esophageal sphincter relaxations (TLESR), i.e. relaxations not triggered by swallows. It has also been shown that gastric acid secretion usually is normal in patients with GERD. Consequently, there is a need for compounds which reduce the incidence of TLESR and thereby prevent reflux.

20

DISCLOSURE OF THE INVENTION

In the applicants' earlier patent application WO 98/11885, filed on 15 September 1997, it is
25   disclosed that GABA$_B$ receptor agonists can be used to reduce the incidence of transient lower esophageal sphincter relaxations (TLESR).

The present invention provides nucleic acid molecules encoding human and canine GABA$_B$ receptors. These nucleic acid molecules will make possible the screening for
30   compounds which are agonists or antagonists of GABA$_B$ receptors, e.g. compounds which are inhibitors of transient lower esophageal sphincter relaxations (TLESR).

Consequently, in a first aspect, the present invention provides a nucleic acid molecule encoding a GABA$_B$ receptor, or a functionally equivalent modified form thereof, said receptor being selected from the group consisting of human and canine GABA$_B$ receptors.

5   In preferred forms of the invention, the said nucleic acid molecule encodes the human GABA$_B$ receptor 1a (SEQ ID NOS: 48 and 49), 1b (SEQ ID NOS: 50 and 51), 1c (SEQ ID NOS: 54 and 55) or 1d (SEQ ID NOS: 56 and 57); or the canine GABA$_B$ receptor 1a (SEQ ID NOS: 52 and 53) or 1c (SEQ ID NOS: 58 and 59). Accordingly, the invention furthermore provides a nucleic acid molecule selected from:

10   (a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO: 48, 50, 52, 54, 56 or 58;

(b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary to the polypeptide coding region of a DNA molecule as defined in (a); and

15   (c) nucleic acid molecules comprising a nucleotide sequence which is degenerate as a result of the genetic code to a nucleotide sequence as defined in (a) or (b).

Furthermore, the invention provides nucleic acid molecules of genomic origin encoding human GABA$_B$ receptors (SEQ ID NOS: 60 and 61) as well as nucleic acid molecules (set

20   forth as SEQ ID NO: 70, 72, 74, 76, 78, 80, 82, 84) encoding additional isoforms of the human GABA$_B$ receptor which isoforms can be shown to be generated by alternative splicing.

It should thus be understood that the nucleic acid molecule according to the invention is

25   not to be limited strictly to molecules comprising the sequences set forth as SEQ ID : 48, 50, 52, 54, 56 or 58. Rather the invention encompasses nucleic acid molecules carrying modifications like substitutions, small deletions, insertions or inversions, which nevertheless encode proteins having substantially the biochemical activity of the GABA$_B$ receptors according to the invention. Included in the invention are consequently nucleic

30   acid molecules, the nucleotide sequence of which is at least 95% homologous, preferably at least 96%, 97%, 98% or 99% homologous, with the nucleotide sequence shown as SEQ ID NO: 48, 50, 52, 54, 56 or 58 in the Sequence Listing.

SUBSTITUTE SHEET (RULE 26)

The term "stringent hybridization conditions" is known in the art from standard protocols (e.g. Current Protocols in Molecular Biology, editors F. Ausubel et al., John Wiley and Sons, Inc. 1994) and could be understood as as stringent or more stringent than those

5   defined by e.g. hybridization to filter-bound DNA in 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at +65°C, and washing in 0.1xSSC / 0.1% SDS at +68°C.

Included in the invention is also a nucleic acid molecule which nucleotide sequence is degenerate, because of the genetic code, to a nucleic acid of the present invention and more

10   particularly to one of the nucleotide sequences set forth as SEQ ID NOs: 48, 50, 52, 54, 56 and 58. A sequential grouping of three nucleotides, a "codon", codes for one amino acid. Since there are 64 possible codons, but only 20 natural amino acids, most amino acids are coded for by more than one codon. This natural "degeneracy", or "redundancy", of the genetic code is well known in the art. It will thus be appreciated that the nucleic acid

15   sequences shown in the Sequence Listing is only an example within a large but definite group of nucleic acid sequences which will encode the polypeptide as described above.

In a further aspect, the invention provides a recombinant polypeptide encoded by a nucleotide sequence of the present invention, encoding a $GABA_B$ receptor. In preferred

20   forms of the inventions, the said polypeptide comprises an amino acid sequence set forth as SEQ ID NO: 49, 51, 53, 55, 57, 59, 71, 73, 75, 77, 79, 81, 83 or 85 in the Sequence Listing. However, polypeptides of the present invention are not to limited to those having an amino acid sequence identical with one of SEQ ID NOs: 49, 51, 53, 55, 59, 71, 73, 75, 77, 79, 81, 83 or 85 in the Sequence Listing. Rather the invention encompasses polypeptides carrying

25   modifications such as substitutions, small deletions, insertions or inversions, which polypeptides nevertheless have substantially the biological activities of the $GABA_B$ receptor. Included in the invention are consequently polypeptides, the amino acid sequence of which is at least 95% homologous, preferably at least 96%, 97%, 98% or 99% homologous, with one of the amino acid sequences described by SEQ ID NOs: 49, 51, 53,

30   55, 57 59, 71, 73, 75, 77, 79, 81, 83 and 85 in the Sequence Listing.

Included in the invention are polypeptides of the present invention which have been post-translationally modified, e.g. by cleavage of an N-terminal signal sequence which can be e.g. 1 to 25 amino acids long.

5   In yet another aspect, the invention provides a vector transformed with a nucleic acid molecule of the present invention. The said vector can e.g. be a replicable expression vector which carries and is capable of mediating the expression of a nucleic acid molecule according to the invention. In the present context the term "replicable" means that the vector is able to replicate in a given type of host cell into which is has been introduced.

10   Examples of vectors are viruses such as bacteriophages, cosmids, plasmids and other recombination vectors. Nucleic acid molecules are inserted into vector genomes by methods well known in the art.

Included in the invention is also a cultured host cell harbouring a vector according to the

15   invention. Such a host cell can be a prokaryotic cell, a unicellular eukaryotic cell or a cell derived from a multicellular organism. The host cell can thus e.g. be a bacterial cell such as an *E. coli* cell; a cell from a yeast such as *Saccharomyces cervisiae* or *Pichia pastoris*, or a mammalian cell. The methods employed to effect introduction of the vector into the host cell are standard methods well-known to a person familiar with recombinant DNA

20   methods.

A further aspect of the invention is a process for production of a $GABA_B$ receptor polypeptide according to the invention, said process comprising culturing a host cell as defined above under conditions whereby the said polypeptide is produced, and recovering

25   the said polypeptide.

A further important aspect of the invention is a method for the screening of compounds which are inhibitors of transient lower esophageal sphincter relaxations (TLESR), said method comprising the use of a nucleic acid molecule encoding a $GABA_B$ receptor. The

30   said nucleic acid molecule encoding a $GABA_B$ receptor can e.g. be one of the nucleic acid molecules according to the invention encoding human or canine $GABA_B$ receptors. However, it should be understood that this aspect of the invention is not limited to the use

of the said human and canine GABA_B receptors, but rather encompasses the use of any

GABA_B receptor for screening for compounds which are inhibitors of transient lower

esophageal sphincter relaxations.

5   In yet another important aspect, the invention provides a method for the screening of

compounds which are agonists or antagonists to a GABA_B receptor, said method

comprising the use of a nucleic acid molecule, according to the invention, encoding human

or canine GABA_B receptors.

10   **Brief Description of the Drawings**

Figure 1: Map of the human GABA_B receptor gene.

The exon/intron organisation is shown. Exons are indicated as solid boxes numbered 1-23.

15   The part of intron 5 that is retained together with exon 6 giving rise to GABA_B receptor 1b

is indicated as an open box.

Figure 2: Expression of human GABA_B receptor 1b isoform in transfected C127 cells.

20

Western blot analysis of transfected C127 cells using a polyclonal anti-human GABA_B

receptor antibody. Lane 1: Untransfected C127 whole cell lysate. Lanes 2-7: Whole cell

lysates of six independent clones transfected with human GABA_B receptor 1b isoform

encoding cDNA. The clones analysed in lanes 4 to 7 express a GABA_B receptor of

25   expected molecular weight (arrow).

Figure 3: Expression of human GABA_B receptor 1d isoform in transfected C127 cells.

30   Western blot analysis of transfected C127 cells using a polyclonal anti-human GABA_B

receptor antibody. Lanes 1-3: Concentrated culture media from three independent C127

clones transfected with a cDNA expression construct encoding the human GABA_B receptor

1d isoform. Lanes 4-6: Whole cell lysates corresponding to the clones analysed in lanes 1-3. The experiment revealed that the human GABA$_B$ receptor 1d cDNA encodes a secreted isoform. The arrow indicates the bands corresponding to the 1d isoform.

5

Figure 4: Expression of human GABA$_B$ receptor 1d isoform in *E. coli*.

Western blot analysis of transformed *E. coli* cells using a polyclonal anti-human GABA$_B$ receptor antibody. Lane 1: Lysate from an uninduced *E. coli* culture transformed with an

10   pET-based expression construct encoding the human GABA$_B$ receptor 1d cDNA. Lane 2: Lysate from an IPTG-induced *E. coli* culture transformed with an expression construct encoding the human GABA$_B$ receptor 1d cDNA. Lane 3: Lysate from an IPTG-induced *E. coli* culture transformed with an expression construct encoding an unrelated protein. Lane 4: The BSA-conjugated peptide previously used for immunization was loaded on the

15   gel as a positive antibody control.

The screening methods according to the invention can e.g. comprise the steps (a) transforming a cultured cell with a nucleic acid molecule encoding a GABA$_B$ receptor, so

20   that a GABA$_B$ receptor is expressed on the surface of the cell; (b) contacting a test compound with the said cell; and (c) determining whether the test compound binds to, and/or activates, the GABA$_B$ receptor.

In particular GABA$_B$ receptor expressing cells, transgenic animals or cells and tissues

25   derived thereof, nay be used to screen substance libraries for antagonist or agonist activities. For this purpose, GABA$_B$ receptor expression may be directed to cells and tissues containing, either naturally or artificially, the necessary components allowing correct receptor transport and processing as well as coupling to second messenger pathways. Screening may be performed as ligand binding assays or functional assays. For

30   screening, cells and tissues my be prepared in various ways, each uniquely suited to its purpose. Ligand binding assays are performed *in vivo* or *in vitro* using e.g. radiolabelled GABA. Functional assays examplified by, but not limited to, Ca^{++}-responses, cAMP-

responses and effects on K^+ channels, may be performed in living cells, broken cells, isolated cell membranes, as well as in tissues and in living animals. To facilitate measurement of physiological GABA$_B$ receptor mediated responses, GABA$_B$ receptors may be co-expressed with promiscous G-proteins like e.g. Gα16 or Gqi5 increasing G-

5   protein coupling. Another possible way to increase G-protein coupling is to fuse the GABA$_B$ receptor with appropriate G-proteins using standard molecular techniques. In order to further improve readouts in Ca^{++}-response assays, GABA$_B$ receptors may be co-expressed with aequorin, a photoprotein cloned from the luminescent jellyfish *Aequorea victoria*.

10

In yet another aspect, the invention provides a pharmaceutical compositions comprising a soluble GABA$_B$ receptor further comprising one or more pharmaceutical acceptable carriers and/or diluents.

15   In yet another aspect, the invention provides a method for the diagnosis or treatment of conditions related to GABA-dysfunction, e.g. epilepsy, psychiatric disorders such as depression and anxiety, cognitive dysfunction, gastroesophageal reflux disease, emesis, irritable bowel syndrome, dyspepsia, spasticity, arthritis, allergies, autoimmune diseases, neoplastic diseases, pain, and infectious diseases, comprising the use or administration of

20   soluble forms of the GABA$_B$ receptor, such as the human GABA$_B$ receptor 1c or 1d or functionally equivalent modified forms thereof; preferably being a polypeptidfe of the present invention..

The soluble forms of the GABA$_B$ receptor can e.g. be produced by culturing a host cell

25   harbouring a vector comprising a nucleic acid encoding the soluble GABA$_B$ receptor under conditions where whereby the said polypeptide is produced, the polypeptide recovered and administered to a patient in need thereof.

30   Furthermore, the level of soluble GABA$_B$ receptors in certain body fluids, e.g. serum and CSF, can be measured and used in diagnostics related to conditions with altered levels of soluble GABA$_B$ receptors in said body fluids.

Throughout this description the terms "standard protocols" and "standard procedures", when used in the context of molecular cloning techniques, are to be understood as protocols and procedures found in an ordinary laboratory manual such as: Current Protocols in Molecular Biology, editors F. Ausubel et al., John Wiley and Sons, Inc. 1994, or Sambrook,

5   J., Fritsch, E.F. and Maniatis, T., Molecular Cloning: A laboratory manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY 1989.

EXAMPLES

10

EXAMPLE 1A: Cloning and sequencing of cDNA encoding human $GABA_B$ receptor 1a and 1b

Messenger RNA from human hippocampus was obtained from Clontech (Palo Alto, CA,

15   USA) (catalog #6578-1). First-strand cDNA synthesis reactions were performed using the First-strand cDNA Synthesis kit from Amersham Pharmacia Biotech (Uppsala, Sweden). The $pd(N)_6$ primer was used to prime the first-strand synthesis. The generated cDNA molecules were used as template in the PCR reactions described below.

20   Specific PCR primers were designed (Table 1) based on the sequences of the rat $GABA_B$ receptor 1a and 1b cDNA (Kaupmann et al. 1997, EMBL accession numbers Y10369 (SEQ ID NO: 44) and Y10370 (SEQ ID NO: 46)).

TABLE 1

Primers used for RT-PCR on mRNA from human hippocampus

Nr.	Species	Sequence 5´- 3´	SEQ ID NO
794	Rat	GTTTCTTCTCGGATCCAGCTGTGCCTG	1
795	Rat	CAGGCACAGCTGGATCCGAGAAGAAACT	2
796	Rat	CGGTCGACTCACTTGTAAAGCAAATGTACTCGACTCCC	3
797	Rat	ATGCGCGCCGGCAGCCAACATGCTGCTGCTGCTGCTGGTGC	4
831	Rat	CGGTCGACTCACTTGTAAAGCAAATGTACTCGACTCCCATCACAGC	5
838	Rat	ATGCGCGCCGGCAGCCAACATGCTGCTGCTGCTGCTGGTGCCTCTCTTCC	6
842	Rat	CAGGCACAGCTGGATCCGAGAAGAAACTCTGTCGGAAAGT	7
863	Rat	GGTCATCCAGCGTTGAGGTGAAGAC	8
864	Rat	GAAGGTTGCCAGATTATACATCCGC	9
865	Rat	CCACGATGATTCGAGCATCTTGACG	10
866	Rat	GCCTCTCACTCCCCTCATCTCC	11
932	Human	GAGTGAAGGAGGCTGGAATTG	12

5   cDNA fragments encoding parts of the human GABA$_B$ receptors were amplified directly

by PCR using the designed primers with the generated cDNA molecules as templates. All

PCR experiments were carried out using the Perkin Elmer Taq DNA polymerase with Gene

Amp (Roche Molecular Systems Inc., NJ, USA) with the following PCR program: +95°C

for 1 minute, +50°C for 30 seconds, +72°C for 3 minutes, repeated 44 times and finally

10   +72°C for 7 minutes. The following primer combinations gave PCR products with

expected sizes: 838 and 842, 838 and 795, 797 and 865, 864 and 865, 864 and 863 which

corresponds to the 5´-end of the GABA$_B$ receptor 1a. Primer pair 932 and 831, 932 and

796, 794 and 831 gave PCR products which correspond to the 3´-end of both GABA$_B$

receptor 1a and 1b. The primer combination 839 and 918 gave a PCR product

15   corresponding to the 5'-end of the GABA$_B$ receptor 1b.

The PCR products were subcloned into the pGEM-T vector from Promega (Madison,

USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide

sequence for all subclones were determined using a Thermo Sequenase dye terminator

20   cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As

primers for sequencing reactions specific oligonucleotides complementary to the vector

pGEM-T or primers complementary to the cDNA encoding the GABA$_B$ receptor were

used.

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Additional PCR primers were designed based on the obtained sequences encoding

fragments of the human GABA$_B$ receptor and additional DNA fragments encoding parts of

the human GABA$_B$ receptors were amplified by PCR, the PCR products subcloned and

5   sequenced as described above.

EXAMPLE 1B : Cloning and sequencing of the 3'-ends of the cDNA encoding human

GABA$_B$ receptors 1a and 1b

10

Messenger RNA from human hippocampus was obtained from Clontech (Palo Alto, CA,

USA) (catalogue #6578-1). First strand cDNA synthesis reactions were performed using

the First-strand cDNA Synthesis kit from Amersham Pharmacia Biotech (Uppsala,

Sweden). The Not I-d(T)$_{18}$ primer was used to prime the first-strand synthesis. The

15   generated cDNA molecules were used as template in the PCR reactions described below.

Specific PCR primers were designed (Table 2) based on the sequences of the human

GABA$_B$ receptor 1a and 1b cDNA obtained in Example 1A and the EST sequence EMBL

accession number Y11044.

20

By homology searches in the EMBL database using the GABA$_B$ receptor cDNA sequences

obtained in Example 1A as query the EST sequence EMBL accession number Y11044

have been found to be homologous to the 3'-end of the GABA$_B$ receptor cDNA.

25   TABLE 2

Primers used in PCR to amplify 3'ends of human GABA$_B$ receptor cDNA

Nr	Species	Sequence 5'- 3'	SEQ ID NO
938	Human	GACGCTTATCGAGCAGCTTC	13
972	Human	AGCCCAGAACTCACAGGGGGACAT	14
973	Human	GCTTCAAGCCAGGTACGAACTAA	15

cDNA fragments encoding parts of the human GABA$_B$ receptors were amplified directly by

30   PCR using the designed primers with the generated cDNA molecules as templates. All

PCR experiments were carried out using the Perkin Elmer Taq DNA polymerase with Gene Amp (Roche Molecular Systems Inc., NJ, USA) with the following PCR program: + 95°C for 1 minute, +50°C for 30 seconds,+72°C for 3 minutes, repeated 44 times and finally +72°C for 7 minutes. The following primer combinations gave PCR products with

5   expected sizes: 938 and 972, 938 and 973 corresponding to the 3´end of both GABA$_B$ receptor 1a and 1b cDNA.

The PCR products were subcloned into the pGEM-T vector from Promega (Madison, USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide

10   sequence for all subclones were determined using a Thermo Sequenase dye terminator cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As primers for sequencing reactions specific oligonucleotides complementary to the vector pGEM-T or primers complementary to the cDNA encoding the GABA$_B$ receptor were used.

15

EXAMPLE 1C : Cloning and sequencing of the 5'-end of the cDNA encoding human GABA$_B$ receptor 1b

20   Messenger RNA from human hippocampus was obtained from Clontech (Palo Alto, CA, USA) (catalogue #6578-1). Marathon cDNA amplification Kit (Clontech) was used for performing 5´/3'- RACE (Rapid Amplification of cDNA Ends). Adaptor-ligated double stranded cDNA molecules were amplified according to the manufacturers description. The pd(N)$_6$ primer from the First-strand cDNA Synthesis kit from Amersham Pharmacia

25   Biotech (Uppsala, Sweden) was used to produce the adaptor-ligated cDNA.

A specific PCR primer was designed (Table 3) based on the sequences of the human GABA$_B$ receptor 1b cDNA obtained in Example 1A.

TABLE 3

Primers used in PCR to amplify the 5'-ends of human GABA_B receptor cDNA

Nr.	Species	Sequence 5'-3'	SEQ ID NO
958	Human	TGGCCCTCCACCGCCTCAGTCATCTCA	16
AP1	Marathon kit	CCATCCTAATACGACTCACTATAGGGC	17

5   cDNA fragments encoding part of the human GABA_B receptors were amplified directly by
PCR using the designed primers with the generated adaptor-ligated cDNA molecules as
template. The PCR experiment was carried out using the Expand Long Template PCR
System (Boehringer Mannheim GmbH, Germany) with the following PCR program: +
$94°C$ for 1minute, + $94°C$ for 30 seconds, $+60°C$ for 30 seconds, $+68°C$ for 4 minutes,

10   repeated 24 times. The primer combination AP1 and 958 gave a PCR product which
corresponded to the 5'-end of the GABA_B receptor 1b cDNA, including 190 base pairs
upstream the initiation codon.

The PCR products were subcloned into the pGEM-T vector from Promega (Madison,
15   USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide
sequence for all subclones were determined using a Thermo Sequenase dye terminator
cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As
primers for sequencing reactions specific oligonucleotides complementary to the vector
pGEM-T or primers complementary to the cDNA encoding the GABA_B receptor were
20   used.

EXAMPLE 1D : Cloning and sequencing of the 5'-end of the cDNA encoding human
GABA_B receptor 1a

25

Messenger RNA from human hippocampus was obtained from Clontech (Palo Alto, USA)
(catalogue #6578-1). Marathon cDNA amplification Kit (Clontech) was used to obtain
adaptor-ligated double stranded cDNA molecules according to the manufacturer's
description. The pd(N)_6 primer from the First-strand cDNA Synthesis kit from Amersham
30   Pharmacia Biotech (Uppsala, Sweden) was used to obtain the adaptor-ligated cDNA .

Specific PCR primers were designed (Table 4) based on the sequences of the human GABA$_B$ receptor 1a cDNA obtained in Example 1 and the rat GABA$_B$ receptor 1a cDNA disclosed in WO 97/46675.

5

TABLE 4

Primers used to amplify 5'-ends of the human GABAB receptor 1a cDNA

Nr.	Species	Sequence 5'-3'	SEQ ID NO
1033	Human	CTCAATCTCATAGTCCACTGG	18
1087	Rat	CCTTGAGGCCCGGGGAGAG	19

10　cDNA fragments encoding part of the human GABAB 1a receptor were amplified directly by PCR using the designed primers with the generated adaptor-ligated cDNA molecules as template. The PCR was performed using the Perkin Elmer Taq DNA polymerase with Gene Amp (Roche Molecular Systems Inc., NJ, USA) with the following PCR program: +94°C for 1 minute, +50°C for 30 seconds,+72°C for 3 minutes; +94°C for 1 minute, +60°C

15　for 30 seconds,+72°C for 4 minutes, repeated 34 times and finally +72°C for 7 minutes.

The primer combination 1087 and 1033 gave a PCR product corresponding to the 5'-end of the GABA$_B$ receptor 1a cDNA , including 26 base pairs upstream the initiation codon.

20　The PCR products were subcloned into the pGEM-T vector from Promega (Madison, USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide sequence for all subclones were determined using a Thermo Sequenase dye terminator cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As primers for sequencing reactions specific oligonucleotides complementary to the vector

25　pGEM-T were used.

A complete cDNA sequence encoding the human GABA$_B$ receptors 1a (SEQ ID NO: 48) and the human GABA$_B$ receptor 1b (SEQ ID NO: 50) were obtained by aligning the sequences of the different fragments cloned and sequenced in Examples 1A, 1B, 1C and

30　1D.

EXAMPLE 2A: Cloning and sequencing of cDNA encoding canine $GABA_B$ receptor 1a

5   QuickPrep Micro mRNA Purification kit (Amersham Pharmacia Biotech, Uppsala, Sweden) was used to isolate mRNA from canine neural tissues according to the manufacturers description. First-strand cDNA synthesis reactions were performed using the First-strand cDNA Synthesis kit from Amersham Pharmacia Biotech (Uppsala, Sweden). The Not-I-d(T)$_{18}$ bifunctional or pd(N)$_6$ primer was used to prime the first-strand synthesis.

10 The generated cDNA molecules were used as template in the PCR reactions described below.

Specific PCR primers (Table 5) were designed based on the sequences of the rat $GABA_B$ receptor 1a and 1b cDNA (Kaupmann et al. 1997, EMBL accession numbers Y10369 (SEQ

15 ID NO: 44 and Y10370 (SEQ ID NO: 46)).

TABLE 5

Primers used for RT-PCR on mRNA from canine cortex

Nr.	Species	Sequence 5´-3´	SEQ ID NO
795	Rat	CAGGCACAGCTGGATCCGAGAAGAAACT	20
831	Rat	CGGTCGACTCACTTGTAAAGCAAATGTACTCGACTCCCATCACAGC	21
838	Rat	ATGCGCGCCGGCAGCCAACATGCTGCTGCTGCTGCTGGTGCCTCTCTTCC	22
840	Rat	CGTCAAGATGCTCGAATCATCG	23
841	Rat	CAGGGGGCTCAGAGGGTCCC	24
842	Rat	CAGGCACAGCTGGATCCGAGAAGAAACTCTGTCGGAAAGT	25
844	Rat	CGGTCGACTCACTTGTAAAGCAAATGTACTCGACTCCCATCACAGCTAAG	26
848	Rat	ACTTTCCGACAGAGTTTCTTCTCGGATCCAGCTGTGCCTG	27
865	Rat	CCACGATGATTCGAGCATCTTGACG	28

20 cDNA fragments encoding parts of the canine $GABA_B$ receptor were amplified directly by PCR using the designed primers with the generated cDNA molecules as templates. All PCR experiments were carried out using the Perkin Elmer Taq DNA polymerase with Gene Amp (Roche Molecular Systems Inc., NJ, USA) with the following PCR program: +95°C

25 for 1 minute, +50°C for 30 seconds, +72°C for 3 minutes, repeated 44 times and finally

+72°C for 7 minutes. The following primer combinations gave PCR products with

expected sizes: 842 and 838, 838 and 795, 838 and 865 which corresponds to the 5´-part of

the canine GABA$_B$ receptor cDNA . Primer pair 848 and 844, 848 and 831, 848 and 841,

840 and 841 gave PCR products which correspond to the 3´-part of the canine GABA$_B$

5   receptor cDNA.

The PCR products were subcloned into the pGEM-T vector from Promega (Madison,

USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide

sequence for all subclones were determined using a Thermo Sequenase dye terminator

10   cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As

primers for sequencing reactions specific oligonucleotides complementary to the vector

pGEM-T or primers complementary to the cDNA encoding the GABA$_B$ receptor were

used.

15

EXAMPLE 2B: Cloning and sequencing of the 3'- and 5'-ends of the cDNA encoding

canine GABA$_B$ receptor 1a

QuickPrep Micro mRNA Purification kit (Amersham Pharmacia Biotech, Uppsala,

20   Sweden) was used to isolate mRNA from canine nerve tissues according to the

manufactures description. Marathon cDNA amplification Kit (Clontech, Palo Alto, CA,

USA) were used for performing both 5´-and 3´-RACE. Two adaptor-ligated double

stranded cDNA libraries were amplified according to the manufacturers description. A

random primer (pd(N)$_6$) was used when amplifying the adaptor-ligated cDNA for the 5´-

25   RACE and the Marathon cDNA Synthesis primer (52-mer) was used when amplifying the

adaptor ligated cDNA for the 3'-RACE.

Specific PCR primers were designed (Table 6) based on the sequence of canine GABA$_B$

receptor 1a cDNA obtained in Example 2A.

30

TABLE 6

Primers used in PCR to amplify the 5'- and 3'-ends of canine GABA$_B$ receptor 1a cDNA

Nr.	Species	Sequence 5´-3´	SEQ ID NO
936	canine	CTACCGCGCAATGAACTCCTCGTC	29
1076	canine	CGAGGTGGCGTTGGGGGTCTGTGC	30
AP1	Marathon kit	CCATCCTAATACGACTCACTATAGGGC	31
AP2	Marathon kit	ACTCACTATAGGGCTCGAGCGGC	32

5   cDNA fragments encoding parts of the canine GABA$_B$ receptor were amplified by PCR
from the adaptor-ligated cDNA using the designed primers. A number of different PCR
programs were tested to find conditions where PCR products corresponding to GABA$_B$
receptor DNA were obtained. The 5´- PCR experiments were carried out using the Expand
Long Template PCR System (Boehringer Mannheim GmbH, Germany) with the following

10   PCR program: +94°C for 30 seconds, +72°C for 3 minutes, repeated 4 times; +94°C for 30
seconds, +70°C for 3 minutes, repeated 4 times; and +94°C for 30 seconds, +68°C for
3minutes, repeated 24 times. The primer combination AP2 and 1076 gave a PCR product
which corresponded to the 5´-end of the GABA$_B$ receptor cDNA, including 114 base pairs
upstream the initiation codon.

15

The 3´- PCR experiments were carried out using the Expand Long Template PCR System
(Boehringer Mannheim GmbH, Germany) with the following PCR program: +94°C for 1
minute; and +94°C for 30 seconds, +60°C for 30 seconds,+68 °C for 4 minutes, repeated
29 times. The primer combination AP1 and 936 gave a PCR fragment which corresponded

20   to the 3´-end of the GABA$_B$ receptor cDNA, including the poly(A) tail.

The PCR products were subcloned into the pGEM-T vector from Promega (Madison,
USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide
sequence for all subclones were determined using a Thermo Sequenase dye terminator

25   cycle sequencing pre-mix kit(Amersham Pharmacia Biotech, Uppsala, Sweden). As
primers for sequencing reactions specific oligonucleotides complementary to the vector
pGEM-T or primers complementary to GABA$_B$ receptor DNA were used.

Complete cDNA sequence encoding the canine GABA$_B$ receptor 1a (SEQ ID NO: 52) was

obtained by aligning the sequences of the different fragments obtained in Example 2A and

Example 2B.

5

EXAMPLE 3A: Cloning of cDNA encoding human GABA$_B$ receptor 1c and 1d from

Jurkat cells

A guanidinisothiocyanate/CsCl method was used to isolate total RNA from Jurkat cells.

10   The first-strand cDNA synthesis was performed using the First-strand cDNA Synthesis kit

from Amersham Pharmacia Biotech (Uppsala, Sweden). The pd(N)$_6$ primer was used to

prime the first strand synthesis. The generated cDNA molecules were used as templates in

the PCR reaction described below.

15   Specific PCR primers (Table 7) were designed based on the sequence of human GABA$_B$

receptor 1a and 1b cDNA (Example 1), rat GABA$_B$ receptor (Kaupmann et al. 1997) and

the EST sequence EMBL accession number Y11044.

TABLE 7

20   Primers used in RT-PCR on mRNA from Jurkat cells

Nr	Species	Sequence 5´-3´	SEQ ID NO
938	human	GACGCTTATCGAGCAGCTTC	33
972	human	AGCCCAGAACTCACAGGGGGACAT	34
973	human	GCTTCAAGCCAGGTACGAACTAA	35
893	rat	GGAGCACCCCCAAGCCCCACTG	36
937	human	CTGGTTCCTCCCAATGTG	37
1005	rat	CCTCTCACTCCCCTCATCTC	38
1030	human	AAGCCAACCTTCCCTGCTTCTC	39

cDNA fragments encoding parts of the GABA$_B$ receptor were amplified directly by PCR

using human and rat specific primers. All PCR experiments were carried out using the

25   Perkin Elmer Taq DNA polymerase with Gene Amp (Roche Molecular Systems Inc., NJ,

USA) with the following PCR program: +95°C for 1 minute; +54°C for 1 minutes, +72°C for 3 minutes, repeated 44 times; and finally +72°C for 7 minutes.

The PCR products were subcloned into the pGEM-T vector from Promega (Madison,

5   USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide sequence for all subclones were determined using a Thermo Sequenase dye terminator cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As primers for sequencing reactions specific oligonucleotides complementary to the vector pGEM-T or primers complementary to GABA$_B$ receptor DNA were used.

10

The following primer combination gave PCR products corresponding to the 3′-end of the GABA$_B$ receptor cDNA: primer pairs 938 and 972; 938 and 973. Unexpectedly both these fragments lacked 149 base pairs, resulting in a frame shift and the insertion of a new termination codon. The following primer combination gave a PCR product corresponding

15   to the 5′-part of the GABA$_B$ receptor 1a cDNA: 893 and 937. The primer pairs 1005 and 937, 1030 and 937 gave PCR products corresponding to the 5′-part of the GABA$_B$ receptor 1b cDNA. Also these PCR fragments lacked the same 149 base pairs which resulted in a frame shift and the insertion of a new termination codon.

20   These results show that Jurkat cells contain mRNA encoding two new forms of the human GABA$_B$ receptor. These are designated GABA$_B$ receptor 1c (SEQ ID NO: 54 and 55) (comprising the same 5'-part as the GABA$_B$ receptor 1a) and GABA$_B$ receptor 1d (SEQ ID NO: 56 and 57) (comprising the same 5'-part as the GABA$_B$ receptor 1b). These two forms of the GABA$_B$ receptor do not contain any of the transmembrane regions and are therefore

25   expected to be soluble forms of the receptor.

EXAMPLE 3B: Analysis of cDNA encoding human GABA$_B$ receptors from hippocampus

30   Messenger RNA from human hippocampus was obtained from Clontech (Palo Alto, USA) (catalogue #6578-1). First strand cDNA synthesis reactions were performed using the First-strand cDNA Synthesis kit from Amersham Pharmacia Biotech (Uppsala, Sweden). The

pd(N)₆ primer was used to prime the first-strand synthesis. The generated cDNA molecules were used as template in the PCR reactions described below.

Specific PCR primer was designed (Table 8) based on the sequences of the cDNAs

5   encoding human GABA$_B$ receptors 1a and 1b.

TABLE 8

Primers used for RT-PCR on mRNA from human hippocampus

Nr	Species	Sequence 5´ - 3´	SEQ ID NO
937	Human	CTGGTTCCTCCCAATGTG	40
938	Human	GACGCTTATCGAGCAGCTTC	41

10

cDNA fragments encoding parts of the human GABA$_B$ receptors were amplified directly by PCR using the designed primers with the generated cDNA molecules as templates. All PCR experiments were carried out using the Perkin Elmer Taq DNA polymerase with Gene Amp (Roche Molecular Systems Inc., NJ, USA) with the following PCR program: +94°C

15   for 1 minute, +50°C for 30 seconds,+72°C for 3 minutes; +94°C for 1 minute, +54°C for 30 seconds, +72°C for 3 minutes repeated 44 times; and finally +72°C for 7 minutes. The primer combination 938 and 937 gave a PCR product which corresponded to the expected size of the GABA$_B$ receptor 1a and 1b cDNA but also a fragment a smaller size.

20   The PCR products were subcloned into the pGEM-T vector from Promega (Madison, USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide sequence for all subclones were determined using a Thermo Sequenase dye terminator cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As primers for sequencing reactions specific oligonucleotides complementary to the vector

25   pGEM-T or primers complementary to the cDNA encoding the GABA$_B$ receptor were used.

The larger PCR fragment was found to correspond to the 3'-part of the GABA$_B$ receptor 1a and 1b cDNA and the smaller fragment which lacked 149 base pairs was found to

30   correspond to the 3'-part of the GABA$_B$ receptors 1c and 1d cDNA identified in Example 3A.

EXAMPLE 4: Cloning and sequencing of cDNA encoding canine GABA$_B$ receptor 1b

5   cDNA encoding the canine GABA$_B$ receptor 1b is isolated in a similar manner as described in Example 2 for receptor 1a. PCR primers specifically designed to be complementary to the 5'-end of the cDNA encoding the rat and human GABA$_B$ receptor 1b, together with PCR primers complementary to the 3'-end of the cDNA encoding the canine GABA$_B$ receptor 1a, and mRNA prepared from a suitable canine tissue, are used.

10

EXAMPLE 5: Cloning of cDNA encoding canine GABA$_B$ receptor 1c

Total RNA from canine liver was prepared using the RNeasy Total RNA Purification
15   Protocols (Quiagen GmbH, Germany). The first-strand cDNA synthesis was performed using the First-strand cDNA Synthesis kit from (Amersham Pharmacia Biotech, Uppsala, Sweden). The pd(N)$_6$ primer was used to prime the first -strand synthesis. The generated cDNA molecules were used as templates in the PCR reaction described below.

20   Specific PCR primers (Table 9) were designed based on the sequence of canine GABA$_B$ receptor 1a cDNA.

TABLE 9

Primers used in RT-PCR

25

Nr	Species	Sequence 5'-3'	SEQ ID NO
936	canine	CTACCGCGCAATGAACTCCTCGTC	42
954	canine	CCTTCTTCTCCTCCTTCTTAGTGA	43

cDNA fragments encoding parts of the canine GABA$_B$ receptor were amplified directly by PCR using canine specific primers. All PCR experiments were carried out using the Perkin Elmer Taq DNA polymerase with Gene Amp (Roche Molecular Systems Inc., NJ, USA)
30   with the following PCR program: +95°C for 1 minute, +54°C for 30 seconds, +72°C for 3

minutes, repeated 44 times and finally +72°C for 7 minutes. The primer combination gave a PCR product with a size corresponding to the GABA$_B$ receptor 1a but also a fragment of smaller size indicating the presence of a GABA$_B$ receptor 1c.

5   The PCR products were subcloned into the pGEM-T vector from Promega (Madison, USA). The inserts were subjected to nucleotide sequence analysis, the complete nucleotide sequence for all subclones were determined using a Thermo Sequenase dye terminator cycle sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As primers for sequencing reactions specific oligonucleotides complementary to the vector

10   pGEM-T were used.

The smaller fragment was shown to lack 149 base pairs. This deletion caused a frame shift and an insertion of a new termination codon, verifying the existence of a canine GABA$_B$ receptor 1c.

15

Complete cDNA sequence encoding the canine GABA$_B$ receptor 1c (SEQ ID NO: 58) was obtained by aligning the sequences of the fragments obtained in Example 2A, Example 2B and Example 5.

20

EXAMPLE 6. Cloning, sequencing and organization of human GABA$_B$ receptor genomic fragments

To determine the structural organization and sequence of the human GABA$_B$ receptor gene,

25   human genomic DNA libraries and human genomic DNA were screened and analyzed. Human genomic libraries were obtained from Clontech (Palo Alto, CA, USA). The libraries were constructed from female leukocyte DNA (catalog # HL1111J), cloned into λEMBL-3 vector. The average size of inserts are 16 kb and the number of independent clones are 1.7×10^6. Human genomic DNA was obtained from Clontech (catalog # 6550-1).

30   In order to isolate recombinant phages containing exon and intron sequences of the human GABA$_B$ receptor gene, 48 individual bacterial plates with a diameter of 150 mm and approximately 4×10^4 individual plaques per plate, were screened. The methods and

solutions used were as described in the Library Protocol Handbook: General Procedures for
the Hybridization of Lambda Phage Libraries w/DNA Probes (Clontech) with some modi-
fications as will be apparent from the following.

5   The experiment was carried out essentially as follows. The numbers are given per plate
     basis. A sample of the phage library diluted in 0.1 ml sterile lambda diluent was prepared
     in order to obtain an estimated titer of 40,000 pfu (plaque forming units). A 0.6 ml LB-
     medium culture of the *E. coli* host strain K802 (obtained from Clontech) was infected with
     40000 pfu recombinant phages for 15 minutes at +37°C. The culture was then mixed with
10   7 ml top agarose (6.5 g of agarose added per liter LB) and poured onto LB plates. The
     plates were incubated at +37°C for approximately 7 hours. The plates were then chilled at
     +4°C.

     Plaque hybridization experiments were as follows. Membrane filters, Colony/Plaque
15   Screen (DuPont, Wilmington, DE, USA), were placed onto the top of the plates for 3
     minutes. For denaturation of DNA the filters were removed and floated in 0.5 M NaOH on
     a plastic wrap for 2 minutes, with the plaque side up. This step was repeated once to ensure
     efficient denaturation. Following neutralization the membrane filters were placed in 1M
     Tris-HCl pH 7.5, two times 2 minutes and allowed to dry.

20

     To obtain probes for DNA hybridization screening of the membrane filters, a GABA$_B$
     receptor cDNA clone was digested with SacII and a 479 bp fragment (base pairs 573-1051
     in the cDNA encoding human GABA$_B$ receptor 1a, SEQ ID NO: 48) was separated by
     agarose electrophoresis, excised and transferred to a polypropylene microcentrifuge tube.
25   Additional probes were obtained by PCR amplification of various regions of the GABA$_B$
     receptor cDNA (base pairs 68-486 and 2368-2863 in the cDNA encoding human GABA$_B$
     receptor 1a, SEQ ID NO: 48). The isolated cDNA fragment was ^{32}P-labeled using
     Megaprime DNA labeling system (Amersham Pharmacia Biotech, Uppsala, Sweden) by
     the following procedure. Water was added at a ratio of 3 ml per gram of gel, and placed in
30   a boiling water bath for 7 minutes to melt the gel and denature the DNA. A volume of
     DNA/agarose solution containing 25 ng of DNA was added to the labeling reaction,
     according to the supplier's instructions. Labeled nucleotides were removed from DNA

labeling reactions using MicroSpin™ G-50 Columns (Amersham Pharmacia Biotech, Uppsala. Sweden).

The DNA hybridization reaction was performed under stringent conditions according to the method described below. The filter membranes were prehybridized at +65°C for at least 1 hour in a solution composed of 1% SDS, 1M NaCl, and 10% dextran sulfate using a hybridization oven (Hybaid Ltd, Ashford, UK). Following prehybridization a solution containing denatured herring sperm DNA of a final concentration of 100 µg/ml and the ^{32}P-labeled DNA probe at a concentration <10 ng/ml (for optimal signal to background ratio) was added to the prehybridization solution and the membrane filters were incubated at +65°C for 10-20 hours. Following the removal of the hybridization solution the membrane filters were first washed in a 2xSSC (0.3M NaCl, 0.03M Na-citrate), 1% SDS solution two times for 5 minutes at room temperature. In the next step, the membrane filters were incubated +60°C two times for 30 minutes each in the same solution. In a third step, the filters were washed two times at room temperature in 0.1xSSC. Finally, the membrane filters were placed on a sheet of filter paper with the DNA face up, and allowed to dry. The dried membrane filters were then exposed to X-ray films and autoradiographed.

Of the approximately $2x10^6$ individual plaques analyzed, four hybridizing plaques were detected and isolated. These three isolates were designated #GR1, #GR12, #GR13 and #GR41, respectively. After several rescreening experiments, the recombinant phage DNA was purified using Qiagen Lambda Midi Kit (Qiagen GmbH, Germany). The purified DNA was digested with SalI and the fragments representing the inserts were isolated by agarose electrophoresis.

The sizes of the inserts were approximately isolate #GR1, 12 kb, isolate #GR12, 12 kb; isolate #GR13, 16kb; and isolate #GR41, 19 kb. These fragments were cloned into SalI digested linearized pUC19, resulting in the plasmids pAM362 (isolate #GR1), pAM363 (isolate #GR12), pAM364 (isolate #GR13)and pAM365 (isolate #GR41). The inserts from the four plaques which hybridizes to the GABA$_B$ receptor cDNA probes were analyzed by PCR, restriction mapping and hybridization to ^{32}P-labeled DNA fragments representing various regions of the GABA$_B$ receptor gene.

The cloned fragments in the plasmids pAM362, pAM363, pAM364 and pAM365 were
characterized by restriction enzyme mapping, using EcoRI, HindIII, PstI, and BamHI. The
approximate positions of the exons and the approximate size of the introns were analyzed

5   and determined by PCR-based exon-exon linking and agarose gel electrophoresis.

In order to facilitate nucleotide sequence analysis, 7 restriction sub-fragments derived from
pAM364, 2 restriction fragments derived from pAM362, and 1 restriction sub-fragment
derived from pAM365 were isolated and cloned into pUC19, resulting in the plasmids

10   pAM366-pAM375. The following strategy was employed; by combining PCR primers
located within the pUC19 sequence either upstream or downstream of the cloning site, with
a PCR primer with defined orientation and specific for the GABA$_B$ receptor derived
subcloned fragment allowed the determination.

15   The inserts in the 10 plasmids pAM366-pAM375 were subjected to nucleotide sequence
analysis. The nucleotide sequences for all subclones were determined using a Thermo
Sequenase dye terminator cycle sequencing pre-mix kit (Amersham Pharmacia Biotech,
Uppsala, Sweden). As primers for sequencing reactions specific oligonucleotides comple-
mentary to pUC19 or primers complementary to the GABA$_B$ receptor cDNA were used.

20

The genomic fragments cloned in the plasmids pAM362-pAM365 where shown to contain
the complete transcribed part of the human GABA$_B$ receptor gene and extends > 3kb
upstream of the first exon and > 2kb downstream of the last exon. The fragments cloned in
the plasmid pAM362 were shown to contain exons 7-11, pAM363 exons 12-22, pAM364

25   exons 1-11, and pAM365 exons 12-23 of the GABA$_B$ receptor gene (Figure 1). The
sequence of exons 1-11 and introns 1-10 is listed in SEQ ID NO: 60 and the sequence of
exons 12-23 and introns 12-22 is listed in SEQ ID NO: 61.

The human GABA$_B$ receptor gene consists of 23 exons and 22 introns (Figure 1). The size

30   of the exons range between 21 bp and 1486 bp. As can be noted from Table 10 exon/intron
boundaries are in accordance with the AG/GT rule and conform well to the consensus
sequence suggested by Mount et al. 1982.

TABLE 10

Exon-Intron boundaries of the GABA$_B$ receptor gene, sequences at exon-intron junctions.

		5´splice donor	3´splice acceptor	
Exon 1-Exon 2	CGAG	GTAAGAG.............................CCGCCTCTCACTTAG		ATGT
Exon 2-Exon 3	GAAG	GTGCATC.............................CGACTCACCCCTTAG		GTTG
Exon 3-Exon 4	TGTG	GTGAGTA.............................CCWATCTCTCCACAG		TCCG
Exon 4-Exon 5	CAGG	GTGAGGG.............................CTTTCCTGCTGCCAG		TGAA
Exon 5-Exon 6	TCAG	GTGAGAT.............................CGCACCCCTCCTCAG		AACG
Exon 6-Exon 7	CAAG	GTAGCCC.............................CCTCTTGTCTTTCAG		TGTG
Exon 7-Exon 8	TGTG	GTAAGCA.............................CTCCCTGCCCCACAG		CTTT
Exon 8-Exon 9	TTCG	GTGAGGA.............................TTATTCCCACCCAAG		ACTC
Exon 9-Exon10	GAAG	GTCAGAT.............................CTTTCTCTGTKGTAG		CGCC
Exon10-Exon11	TGAG	GTGGART.............................CTCCTCTGTATTCAG		GTGT
Exon11-Exon12	CATG	GTGAGAG.............................TTTTTTCCTCCCAAG		ACAT
Exon12-Exon13	CTCT	GTGAGTT.............................TGTTCCTTCCCTCAG		GGCC
Exon13-Exon14	CAGG	GTTAGTA.............................TTGTCGTCTGCCCAG		GTGG
Exon14-Exon15	ATTG	GTGAGTG.............................CCCTGTGCCATGCAG		GAGG
Exon15-Exon16	TCCG	GTXAGTT.............................CCACCTCTGCCCTAG		TTAT
Exon16-Exon17	CCAG	GTGAGGA.............................TCTCTTCCTTTCTAG		GCCC
Exon17-Exon18	GAAG	GTGAGCT.............................CACATATTTATCCAG		ACTC
Exon18-Exon19	TGAG	GTACCAC.............................TYGTTTCTGCCCTAG		ACAT
Exon19-Exon20	CTTG	GTGTGTG.............................CTCCTGCCATCCTAG		GCAT
Exon20-Exon21	GGCA	GTGAGCA.............................TGTCTTTCCCTCTAG		GTCC
Exon21-Exon22	CAAG	GTAAGGA.............................AACATTTGCCCCCAG		ATGC
Exon22-Exon23	TGAG	GTGCGGG.............................TGCTTCTTCCTCCAG		AAAG

5

A comparison of the sequences of the different forms of the human GABA$_B$ receptor
cDNA (SEQ ID NO: 48, 50, 54, and 56) and the sequence of the human GABA$_B$ gene
(SEQ ID NO: 60 and 61) reveals that different mRNA encoding human GABA$_B$ receptors

10   are formed by alternative splicing. The translational start of the GABA$_B$ receptor 1a is
localized in exon 2 and the translational stop is localized in exon 23. The mRNA encoding
GABA$_B$ receptor 1b is formed by alternative splicing where part of intron 5 is retained
together with exon 6 where the translational start of the GABA$_B$ receptor 1b is derived
from the intron sequence. The mRNA encoding GABA$_B$ receptor 1c is formed by

15   alternative splicing where exon 15 are removed together with introns 14 and 15 and a
frame shift and a translational stop are generated in the sequence corresponding to exon 16.

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The mRNA encoding GABA$_B$ receptor 1d is formed when the translational start of the GABA$_B$ receptor 1b is generated together with the translational stop of the GABA$_B$ receptor 1c.

5   The 1a isoform is formed by splicing exon 5 to a cryptic splice site in the middle of exon 6. Transcription of 1b isoform mRNA is most likely initiated from regulatory elements in intron 5. The ATG initiating translation of 1b mRNA is located in the 5'-end of exon 6.

Additional variants of the mRNA encoding variants of the human GABA$_B$ receptor can be
10   derived by alternative splicing where one ore more of the exons or part of exons are excised in the processing of the pre-mRNA. The subsequent transcription of these mRNA will give rise to variants of the human GABA$_B$ receptor with potentially different biological and/or pharmacological activities.

15

EXAMPLE 7. Analysis of cDNA encoding human GABA$_B$ receptors from human brain

Messenger RNA from human fetal brain (catalog #6525-1) and adult human brain (catalog #6516-1) were obtained from Clontech (Palo Alto, CA, USA). First strand cDNA synthesis
20   reactions were performed using the first strand cDNA Synthesis kit from Amersham Pharmacia Biotech (Uppsala, Sweden).The pd(N)$_6$ primer was used to prime the first-strand synthesis. The generated cDNA molecules were used as templates in the PCR reactions described below.

25   Specific PCR primers was designed (Table 11) based on the sequences of the rat GABA$_B$ receptor 1a and 1b cDNA and human GABA$_B$ receptor 1a and 1b cDNA

TABLE 11

Primers used for RT-PCR on mRNA from human fetal brain

Nr	Species	Sequence 5′-3′	SEQ ID NO
838	Rat	ATGCGCGCCGGCAGCCAACATGCTGCTGCTGCTGCTGGTGCCTCT CTTCC	62
863	Rat	GGTCATCCAGCGTTGAGGTGAAGAC	63
864	Rat	GAAGGTTGCCAGATTATACATCCGC	64
865	Rat	CCACGATGATTCGAGCATCTTGACG	65
937	Human	CTGGTTCCTCCCAATGTG	66
1015	Human	CCAGTGGACTATGAGATTGAG	67

5   cDNA fragments encoding parts of the human GABA$_B$ receptors were amplified directly by

PCR using the designed primers with the generated cDNA molecules as templates. PCR

experiments with primers 838, 863 ,864 and 865 were carried out using the Perkin Elmer

Taq DNA polymerase with Gene Amp (Roche Molecular System Inc., NJ, USA) with the

following PCR program: +95°C for 1 minute, +50°C for 30 seconds,+72°C for 3 minutes,

10 repeated 44 times and finally +72°C for 7 minutes. PCR experiments with primers 937 and

1015 were carried out using the Expand Long Template PCR System (Boehringer

Mannheim GmbH, Germany) with the following PCR program: +94°C for 2 minutes;

+94°C for 10 seconds, +55°C for 30 seconds, +68°C for 3 minutes repeated 35 times; and

finally +68°C for 7 minutes. The primer combinations 838 and 863, 864 and 863 , 864 and

15 865, 937 and 1015 gave PCR products.

The PCR products were subcloned into the pGEM-T vector from Promega (Madison, WI,

USA). The inserts were subjected to nucleotide sequence analysis. The complete nucleotide

sequence for all subclones were determined using a ThermoSequenase dye terminator cycle

20 sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As for primers

for sequencing reactions specific oligonucleotides complementary to the vector pGEM-T or

primers complementary to the cDNA encoding the GABA$_B$ receptor were used.

A number of analyzed clones isolated from fetal brain were found to lack 186 base pairs,

25 corresponding to exon 4. This alternative splicing resulted in a cDNA (SEQ ID NO: 70)

encoding a protein (SEQ ID NO: 71) comprising of 899 amino acids and designated GABA$_B$ receptor 1e.

Other clones from fetal brain lacked 368 base pairs, corresponding to exons 4, 5 and 6,

5   resulting in a cDNA (SEQ ID NO: 72) where a frame shift and a translational stop codon are generated in the sequence corresponding to exon 7, encoding a protein (SEQ ID NO: 73) comprising only 97 amino acids designated GABA$_B$ receptor 1f.

One clone lacked 207 base pairs, corresponding to exons 4 and 5, resulting in a cDNA

10   (SEQ ID NO: 74) encoding a protein (SEQ ID NO: 75) comprising 892 amino acids designated GABA$_B$ receptor 1g.

Another clone had two deletions, the first comprising 186 base pairs corresponding to exon 4, the second comprising 39 base pairs corresponding to part of exon 6, resulting in a

15   cDNA (SEQ ID NO: 76) encoding a protein (SEQ ID NO: 77) comprising 886 amino acids designated GABA$_B$ receptor 1h.

Yet another clone from adult human brain was found to have a long deletion comprising 1194 base pairs corresponding to base pairs 319 - 1512 of the cDNA encoding human

20   GABA$_B$ receptor 1a. This deletion corresponds to part of exon 4, exons 5-11, and part of exon 12. This cDNA (SEQ ID NO: 78) encodes a protein (SEQ ID NO: 79) comprising 563 amino acids designated GABA$_B$ receptor 1i.

One clone isolated from fetal brain lacked 284 base pairs corresponding to part of exon 3

25   and the whole exon 4, generating a frame shift and a translational stop codon in the sequence corresponding to exon 5. This cDNA (SEQ ID NO: 80) encodes a protein (SEQ ID NO: 81) comprising only 105 amino acids designated GABA$_B$ receptor 1j.

30   EXAMPLE 8. Analysis of cDNA encoding human GABA$_B$ receptors from Jurkat cells

A guanidinisothiocyanate/CsCl method was used to isolate total RNA from Jurkat cells. First strand cDNA synthesis reactions were performed using the first strand cDNA

Synthesis kit from Amersham Pharmacia Biotech (Uppsala, Sweden).The pd(N)₆ primer

was used to prime the first-strand synthesis. The generated cDNA molecules were used as

templates in the PCR reactions described below.

5   Specific PCR primers was designed (Table 12) based on the sequences of the human

GABA$_B$ receptor 1a and 1b cDNA

TABLE 12

Primers used for RT-PCR on mRNA from Jurkat cells

10

Nr	Species	Sequence 5´-3´	SEQ ID NO
937	Human	CTGGTTCCTCCCAATGTG	68
1015	Human	CCAGTGGACTATGAGATTGAG	69

cDNA fragments encoding parts of the human GABA$_B$ receptors were amplified directly by

PCR using the designed primers with the generated cDNA molecules as templates. The

PCR experiment was carried out using the Expand Long Template PCR System

15   (Boehringer Mannheim GmbH, Germany) with the following PCR program: +94°C for 2

minutes; +94°C for 10 seconds, +55°C for 30 seconds, +68°C for 3 minutes repeated 35

times; and finally +68°C for 7 minutes. The primer combination 937 and 1015 gave a PCR

product.

20   The PCR products were subcloned into the pGEM-T vector from Promega (Madison, WI,

USA). The inserts were subjected to nucleotide sequence analysis. The complete nucleotide

sequence for all subclones were determined using a ThermoSequenase dye terminator cycle

sequencing pre-mix kit (Amersham Pharmacia Biotech, Uppsala, Sweden). As for primers

for sequencing reactions specific oligonucleotides complementary to the vector pGEM-T or

25   primers complementary to the cDNA encoding the GABA$_B$ receptor were used.

Two clones had two deletions, the first comprising 368 base pairs corresponding to exons

4, 5 and 6, the second comprising 151 base pairs corresponding to exon 15 where a frame

shift and a translational stop codon are generated in the sequence corresponding to exon 7.

30   This cDNA (SEQ ID NO: 82) encodes a protein (SEQ ID NO: 83) comprising only 98

amino acids designated GABA$_B$ receptor 1k which is identical to the GABA$_B$ receptor 1f described above.

Another two clones also had two deletions, the first comprising 246 base pairs corresponding to part of exon 4, exon 5 and exon 6, the second comprising 149 base pairs corresponding to exon 15, generating a frame shift and a translational stop codon in the sequence corresponding to exon 16. This cDNA (SEQ ID NO: 84) encodes a protein (SEQ ID NO: 5) comprising 496 amino acids designated GABA$_B$ receptor 1l.

Additional variants of cDNA encoding the human GABA$_B$ receptors can be identified in a similar manner using PCR primers based on the sequence of the cDNA and genomic fragments encoding the human GABA$_B$ receptors disclosed in the present application.

The biological activity of these variants of the human GABA$_B$ receptor can be evaluated by transfection of suitable host cells with expression vectors comprising the corresponding cDNA sequences and subsequent measurement of binding of labeled ligands or activation of the receptor or modulation of receptor function.

EXAMPLE 9: Generation of antibodies

Antibodies were raised in rabbits against four different BSA-conjugated 20 amino acids long synthetic peptides corresponding to selected regions of the human and canine GABA$_B$ receptor extracellular domain. Two were directed against a sequence common for GABA$_B$ receptor 1a and b (ab1 and ab2), one against a GABA$_B$ receptor 1a-specific region (a1) and one against a GABA$_B$ receptor 1b-specific sequence (b1). To allow BSA-conjugation, a cystein residue was added to the N-terminus in all peptides but a1, which contains an endogenous cystein.

Peptide a1: (SEQ ID NO: 49 amino acids 18-37)
       Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile Ile His Pro Pro Trp

Peptide ab1: (SEQ ID NO: 49 amino acids 197-216 with N-terminally added Cys)

     Cys - Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu Ile

His His

5   Peptide ab2:   (SEQ ID NO: 49 amino acids 271-290 with N-terminally added Cys)

     Cys - Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro

Ser Ala

Peptide b1: (SEQ ID NO: 57 amino acids 30-47 with N-terminally added Cys)

10   Cys - Ser His Ser Pro His Leu Pro Arg Pro His Ser Arg Val Pro Pro His Pro Ser

The antibodies were purified from rabbit serum by affinity chromatography using the
corresponding immobilized peptide and subsequently used to detect expression of
recombinant GABA$_B$ receptor isoforms on Western blots.

15

EXAMPLE 10: Heterologous expression of GABA$_B$ receptor isoforms in mammalian cells

A HindIII / SalI cDNA fragment encoding the human GABA$_B$ receptor 1b isoform was

20   cloned into a BPV (bovine papilloma virus)-based expression vector containing the mMT-
1 (murine metallothioneine) promoter. Using the calcium phosphate method, murine C127
cells were co-transfected with the GABA$_B$ receptor expression construct and an expression
plasmid containing a G418 resistance marker gene using the calcium phosphate method.
G418 resistant clones were evaluated by Western blot analysis for expression of the

25   approximately 100 kDa GABA$_B$ receptor 1b isoform(Figure 2). Similarly, but using
Lipofectamine (Life Technologies Inc, Rockville, MD, USA) for transfection, the human
GABA$_B$ receptor 1b isoform was expressed in human HEK-293 cells using the pCI-neo
expression vector. The identity of the heterologously expressed receptor was verified in
HEK-293 cells by Western blot analysis and radiologand binding experiments.

30

A cDNA fragment encoding the human GABA$_B$ receptor 1d isoform was cloned into a
BPV-based expression vector containing the mMT-1 promotor. Using the calcium
phosphate method, murine C127 cells were co-transfected with the GABA$_B$ receptor

expression construct and an expression plasmid containing a G418 resistance marker gene.
G418 resistant clones, and concentrated medium from the same clones, were evaluated for
GABA_B receptor 1d isoform expression by Western blot analysis (Figure 3). The
experiment revealed the human GABA_B receptor 1d to be a secreted isoform.

5

EXAMPLE 11: Heterologous expression of GABA_B receptor isoforms in *E. coli*

A cDNA fragment encoding the human GABA_B receptor 1d isoform was cloned into a
10   modified pET (Pharmacia Amersham, Uppsala, Sweden) vector downstream of a STII
(heat stable enterotoxin II of *E. coli*) signal peptide and followed by a thrombin clevage site
and a hexahistidine tag. The expression construct was subsequently used to transform the
BL21 (DE3) *E. coli* strain. Western blot analysis of IPTG-induced bacteria revealed
expression of a human GABA_B receptor 1d isoform of expected size(Figure 4).

15

In addition, the human GABA_B receptor 1d isoform was successfully expressed without
fusion to a bacterial signal peptide in *E. coli* strain AD494 (DE3).

20   EXAMPLE 12: Method for the screening of substances which are GABA_B receptor
antagonists or agonists

GABA_B receptor expressing cells, transgenic animals or cells and tissues derived thereof,
are used to screen substance libraries for antagonist or agonist activities. Screening is
25   performed as ligand binding assays or functional assays. For screening, cells and tissues are
prepared in various ways, each uniquely suited to its purpose. Ligand binding assays are
performed *in vivo* or *in vitro*. Functional assays exemplified by, but not limited to, Ca^{++}-
responses, cAMP-responses and effects on Cl^- and K^+ channels, are performed in living
cells, broken cells, isolated cell membranes, as well as in tissues and in living animals.

CLAIMS

5

1. A nucleic acid molecule encoding a human or canine GABA$_B$ receptor, or a functionally equivalent modified form thereof.

2. A nucleic acid molecule according to claim 1 encoding a human GABA$_B$ receptor, or a functionally equivalent modified form thereof.

10

3. A nucleic acid molecule according to claim 2 encoding the human GABA$_B$ receptor 1a, or a functionally equivalent modified form thereof.

4. A nucleic acid molecule according to claim 3 selected from:
(a) a nucleic acid molecule comprising a nucleotide sequence set forth as SEQ ID NO: 48;

15

(b) a nucleic acid molecule comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary to the polypeptide coding region of a DNA molecule as defined in (a); and
(c) a nucleic acid molecule comprising a nucleotide sequence which is degenerate as a result of the genetic code to a nucleotide sequence as defined in (a) or (b).

20

5. A nucleic acid molecule according to claim 2 encoding the human GABA$_B$ receptor 1b, or a functionally equivalent modified form thereof..

6. A nucleic acid molecule according to claim 5 selected from:

25

(a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO: 50;
(b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary the polypeptide coding region of a DNA molecule as defined in (a); and

30

(c) nucleic acid molecules comprising a nucleotide sequence which is degenerate as a result of the genetic code to a nucleotide sequence as defined in (a) or (b).

7.   A nucleic acid molecule according to claim 2 encoding the human GABA$_B$ receptor
      1c, or a functionally equivalent modified form thereof.

8.   A nucleic acid molecule according to claim 7 selected from:
5   (a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO:
      54;
      (b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing,
      under stringent hybridization conditions, to a nucleotide sequence complementary the
      polypeptide coding region of a DNA molecule as defined in (a); and
10   (c) nucleic acid molecules comprising a nucleotide sequence which is degenerate as a
      result of the genetic code to a nucleotide sequence as defined in (a) or (b).

9.   A nucleic acid molecule according to claim 2 encoding the human GABA$_B$ receptor
      1d, or a functionally equivalent modified form thereof..

15

10.   A nucleic acid molecule according to claim 9 selected from:
      (a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO:
      56;
      (b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing,
20   under stringent hybridization conditions, to a nucleotide sequence complementary the
      polypeptide coding region of a DNA molecule as defined in (a); and
      (c) nucleic acid molecules comprising a nucleotide sequence which is degenerate as a
      result of the genetic code to a nucleotide sequence as defined in (a) or (b).

25 11.   A nucleic acid molecule according to claim 1 encoding a canine GABA$_B$ receptor, or
          a functionally equivalent modified form thereof.

12.   A nucleic acid molecule according to claim 11 encoding the canine GABA$_B$ receptor
      1a, or a functionally equivalent modified form thereof.

30

13.   A nucleic acid molecule according to claim 12 selected from

(a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO: 52;

(b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary the polypeptide coding region of a DNA molecule as defined in (a); and

(c) nucleic acid molecules comprising a nucleotide sequence which is degenerate as a result of the genetic code to a nucleic acid sequence as defined in (a) or (b).

14   A nucleic acid molecule according to claim 11 encoding the canine $GABA_B$ receptor 1c, or a functionally equivalent modified form thereof.

15.   A nucleic acid molecule according to claim 14 selected from

(a) nucleic acid molecules comprising a nucleotide sequence set forth as SEQ ID NO: 58;

(b) nucleic acid molecules comprising a nucleotide sequence capable of hybridizing, under stringent hybridization conditions, to a nucleotide sequence complementary the polypeptide coding region of a DNA molecule as defined in (a); and

(c) nucleic acid molecules comprising a nucleotide sequence which is degenerate as a result of the genetic code to a nucleic acid sequence as defined in (a) or (b).

16.   A recombinant polypeptide encoded by a nucleotide sequence according to any one of claims 1 to 15.

17.   The polypeptide according to claim 16 comprising an amino acid sequence set forth as SEQ ID NO: 49, 51, 53, 55, 57 or 59 in the Sequence Listing.

18.   A polypeptide according to claim 16 which has been posttranslationally modified.

19.   A vector transformed with a nucleic acid molecule according to any one of claims 1 to 15.

20.   A cultured host cell harboring a vector according to claim 19.

21. A process for the production of a $GABA_B$ receptor, said process comprising culturing a host cell according to claim 20 under conditions whereby the said polypeptide is produced, and recovering the said polypeptide.

5

22. A method for the screening of compounds which are inhibitors of transient lower esophageal sphincter relaxations, said method comprising the use of a nucleic acid molecule encoding a $GABA_B$ receptor.

10   23. A method according to claim 22 wherein the said nucleic acid molecule encoding a $GABA_B$ receptor is the nucleic acid molecule according to any one of claims 1 to 15.

24. A method for the screening of compounds which are agonists or antagonists to a $GABA_B$ receptor, said method comprising the use of a nucleic acid molecule

15   according to any one of claims 1 to 15.

25. A method according to any one of claims 22 to 24 comprising the steps (a) transforming a cultured cell with a nucleic acid molecule encoding a $GABA_B$ receptor, so that a $GABA_B$ receptor is expressed on the surface of the cell; (b)

20   contacting a test compound with the said cell; and (c) determining whether the test compound binds to, and/or activate, the $GABA_B$ receptor.

26. A pharmaceutical compositions comprising a soluble $GABA_B$ receptor further comprising one or more pharamceutical acceptable carriers and/or diluents.

1/2
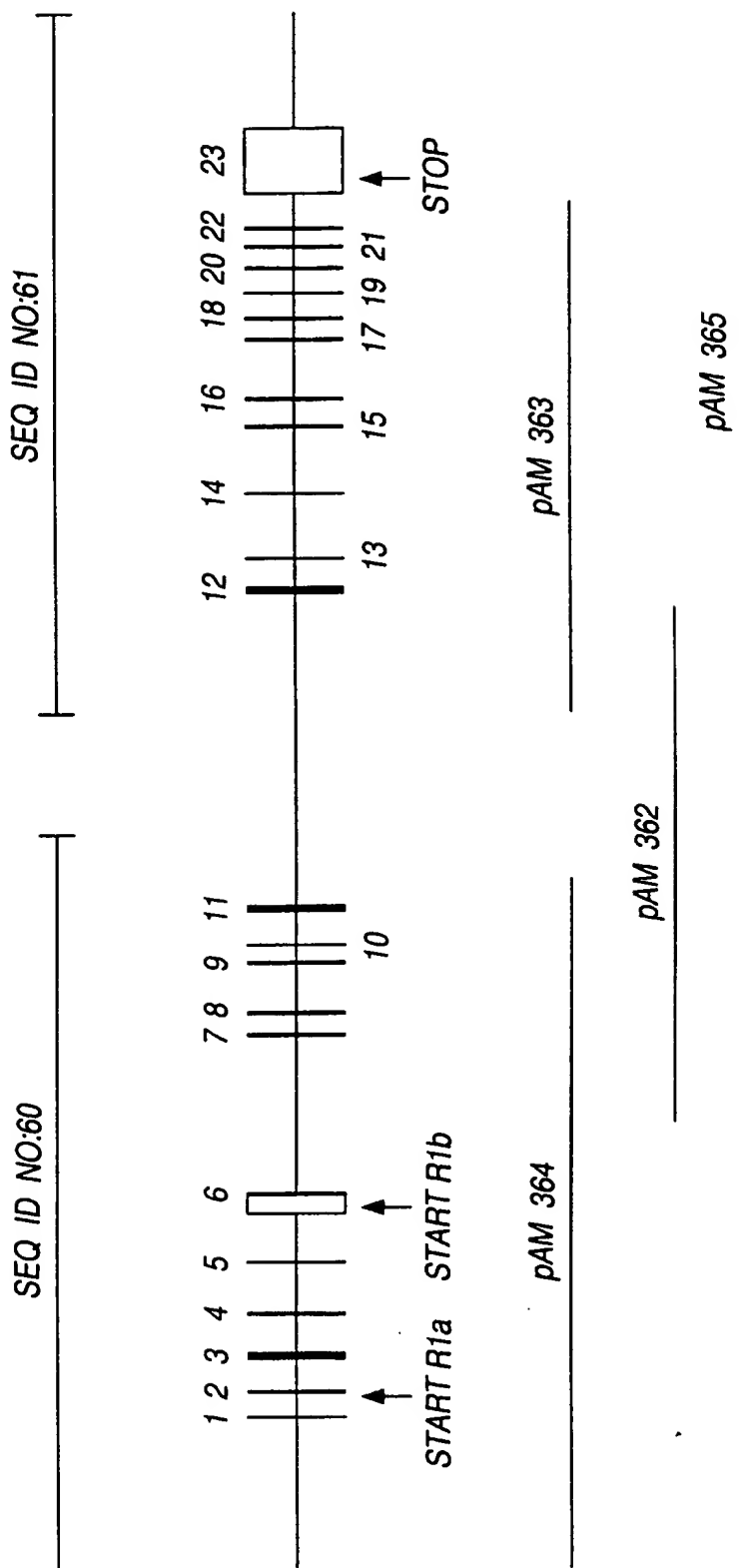
Fig.1

2/2
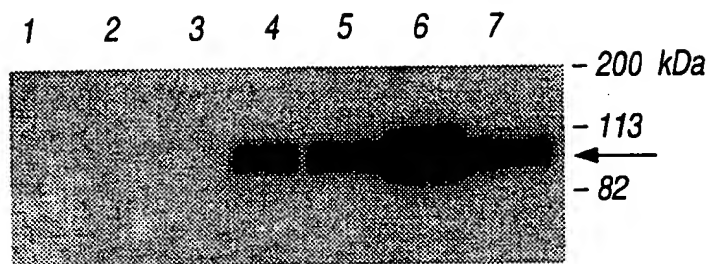
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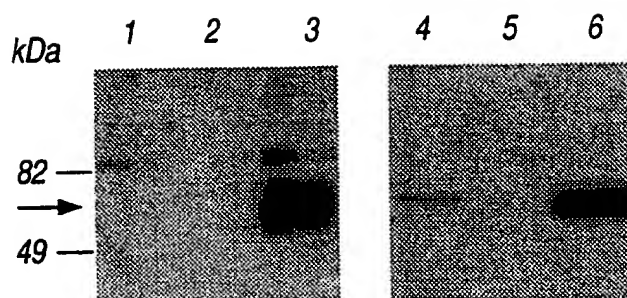
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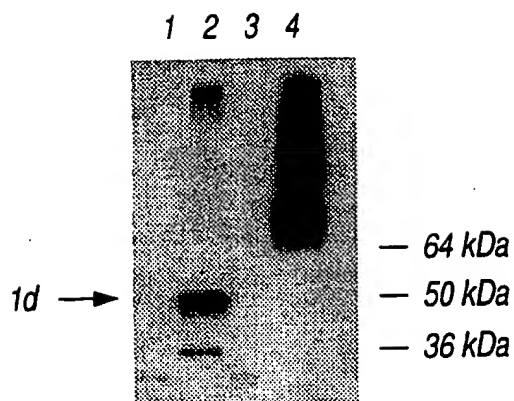
Fig.4

SEQUENCE LISTING

(1) GENERAL INFORMATION:

    (i) APPLICANT:
        (A) NAME: ASTRA AB
        (B) STREET: Västra Mälarehamnen 9
        (C) CITY: Södertälje
        (E) COUNTRY: Sweden
        (F) POSTAL CODE (ZIP): S-151 85
        (G) TELEPHONE: +46-8-553 260 00
        (H) TELEFAX: +46-8-553 288 20
        (I) TELEX: 19237 astra s

    (ii) TITLE OF INVENTION: New nucleotide sequences

    (iii) NUMBER OF SEQUENCES: 85

    (iv) COMPUTER READABLE FORM:
        (A) MEDIUM TYPE: Floppy disk
        (B) COMPUTER: IBM PC compatible
        (C) OPERATING SYSTEM: PC-DOS/MS-DOS
        (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(2) INFORMATION FOR SEQ ID NO: 1:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 27 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

GTTTCTTCTC GGATCCAGCT GTGCCTG   27

H1865-1 WO SEQ   1

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:

    (A) LENGTH: 28 base pairs

    (B) TYPE: nucleic acid

    (C) STRANDEDNESS: single

    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

CAGGCACAGC TGGATCCGAG AAGAAACT   28

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

    (A) LENGTH: 38 base pairs

    (B) TYPE: nucleic acid

    (C) STRANDEDNESS: single

    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

CGGTCGACTC ACTTGTAAAG CAAATGTACT CGACTCCC   38

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

    (A) LENGTH: 41 base pairs

    (B) TYPE: nucleic acid

    (C) STRANDEDNESS: single

    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

ATGCGCGCCG GCAGCCAACA TGCTGCTGCT GCTGCTGGTG C   41

5   (2) INFORMATION FOR SEQ ID NO: 5:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 46 base pairs
            (B) TYPE: nucleic acid
10   (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

15   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CGGTCGACTC ACTTGTAAAG CAAATGTACT CGACTCCCAT CACAGC   46

20   (2) INFORMATION FOR SEQ ID NO: 6:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 50 base pairs
            (B) TYPE: nucleic acid
25   (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

30   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

ATGCGCGCCG GCAGCCAACA TGCTGCTGCT GCTGCTGGTG CCTCTCTTCC   50

35   (2) INFORMATION FOR SEQ ID NO: 7:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 40 base pairs
            (B) TYPE: nucleic acid
40   (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

CAGGCACAGC TGGATCCGAG AAGAAACTCT GTCGGAAAGT   40

(2) INFORMATION FOR SEQ ID NO: 8:

    (i) SEQUENCE CHARACTERISTICS:

        (A) LENGTH: 25 base pairs

        (B) TYPE: nucleic acid

        (C) STRANDEDNESS: single

        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

GGTCATCCAG CGTTGAGGTG AAGAC   25

(2) INFORMATION FOR SEQ ID NO: 9:

    (i) SEQUENCE CHARACTERISTICS:

        (A) LENGTH: 25 base pairs

        (B) TYPE: nucleic acid

        (C) STRANDEDNESS: single

        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

GAAGGTTGCC AGATTATACA TCCGC   25

(2) INFORMATION FOR SEQ ID NO: 10:

    (i) SEQUENCE CHARACTERISTICS:

        (A) LENGTH: 25 base pairs

        (B) TYPE: nucleic acid

        (C) STRANDEDNESS: single

        (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

CCACGATGAT TCGAGCATCT TGACG   25

(2) INFORMATION FOR SEQ ID NO: 11:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 22 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

GCCTCTCACT CCCCTCATCT CC   22

(2) INFORMATION FOR SEQ ID NO: 12:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 21 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

GAGTGAAGGA GGCTGGAATT G   21

(2) INFORMATION FOR SEQ ID NO: 13:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 20 base pairs
        (B) TYPE: nucleic acid

H1865-1 WO SEQ   5

            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: DNA

5

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

GACGCTTATC GAGCAGCTTC   20

10

    (2) INFORMATION FOR SEQ ID NO: 14:

        (i) SEQUENCE CHARACTERISTICS:

15   (A) LENGTH: 24 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

20   (ii) MOLECULE TYPE: DNA

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

AGCCCAGAAC TCACAGGGGG ACAT   24

25

    (2) INFORMATION FOR SEQ ID NO: 15:

        (i) SEQUENCE CHARACTERISTICS:

30   (A) LENGTH: 23 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

35   (ii) MOLECULE TYPE: DNA

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

GCTTCAAGCC AGGTACGAAC TAA   23

40

    (2) INFORMATION FOR SEQ ID NO: 16:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 27 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

TGGCCCTCCA CCGCCTCAGT CATCTCA   27

(2) INFORMATION FOR SEQ ID NO: 17:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 27 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

CCATCCTAAT ACGACTCACT ATAGGGC   27

(2) INFORMATION FOR SEQ ID NO: 18:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 21 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

CTCAATCTCA TAGTCCACTG G   21

H1865-1 WO SEQ   7

(2) INFORMATION FOR SEQ ID NO: 19:

    (i) SEQUENCE CHARACTERISTICS:

        (A) LENGTH: 19 base pairs

        (B) TYPE: nucleic acid

        (C) STRANDEDNESS: single

        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

CCTTGAGGCC CGGGGAGAG   19

(2) INFORMATION FOR SEQ ID NO: 20:

    (i) SEQUENCE CHARACTERISTICS:

        (A) LENGTH: 28 base pairs

        (B) TYPE: nucleic acid

        (C) STRANDEDNESS: single

        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

CAGGCACAGC TGGATCCGAG AAGAAACT   28

(2) INFORMATION FOR SEQ ID NO: 21:

    (i) SEQUENCE CHARACTERISTICS:

        (A) LENGTH: 46 base pairs

        (B) TYPE: nucleic acid

        (C) STRANDEDNESS: single

        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

CGGTCGACTC ACTTGTAAAG CAAATGTACT CGACTCCCAT CACAGC   46

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 50 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

ATGCGCGCCG GCAGCCAACA TGCTGCTGCT GCTGCTGGTG CCTCTCTTCC   50

(2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 22 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:

CGTCAAGATG CTCGAATCAT CG   22

(2) INFORMATION FOR SEQ ID NO: 24:

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 20 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

CAGGGGGCTC AGAGGGTCCC   20

(2) INFORMATION FOR SEQ ID NO: 25:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 40 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

CAGGCACAGC TGGATCCGAG AAGAAACTCT GTCGGAAAGT   40

(2) INFORMATION FOR SEQ ID NO: 26:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 50 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

CGGTCGACTC ACTTGTAAAG CAAATGTACT CGACTCCCAT CACAGCTAAG   50

(2) INFORMATION FOR SEQ ID NO: 27:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 40 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

ACTTTCCGAC AGAGTTTCTT CTCGGATCCA GCTGTGCCTG   40

(2) INFORMATION FOR SEQ ID NO: 28:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 25 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

CCACGATGAT TCGAGCATCT TGACG   25

(2) INFORMATION FOR SEQ ID NO: 29:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 24 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

CTACCGCGCA ATGAACTCCT CGTC   24

(2) INFORMATION FOR SEQ ID NO: 30:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 24 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

5

CGAGGTGGCG TTGGGGGTCT GTGC   24

(2) INFORMATION FOR SEQ ID NO: 31:

10

      (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 27 base pairs
         (B) TYPE: nucleic acid
         (C) STRANDEDNESS: single
15   (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:

20

CCATCCTAAT ACGACTCACT ATAGGGC   27

(2) INFORMATION FOR SEQ ID NO: 32:

25

      (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 23 base pairs
         (B) TYPE: nucleic acid
         (C) STRANDEDNESS: single
30   (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

35

ACTCACTATA GGGCTCGAGC GGC   23

(2) INFORMATION FOR SEQ ID NO: 33:

40

      (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 20 base pairs
         (B) TYPE: nucleic acid

          (C) STRANDEDNESS: single

          (D) TOPOLOGY: linear

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

GACGCTTATC GAGCAGCTTC   20

(2) INFORMATION FOR SEQ ID NO: 34:

     (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 24 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

AGCCCAGAAC TCACAGGGGG ACAT   24

(2) INFORMATION FOR SEQ ID NO: 35:

     (i) SEQUENCE CHARACTERISTICS:
          (A) LENGTH: 23 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:

GCTTCAAGCC AGGTACGAAC TAA   23

(2) INFORMATION FOR SEQ ID NO: 36:

     (i) SEQUENCE CHARACTERISTICS:

           (A) LENGTH: 22 base pairs

           (B) TYPE: nucleic acid

           (C) STRANDEDNESS: single

           (D) TOPOLOGY: linear

5

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

10   GGAGCACCCC CAAGCCCCAC TG   22

    (2) INFORMATION FOR SEQ ID NO: 37:

15   (i) SEQUENCE CHARACTERISTICS:

           (A) LENGTH: 18 base pairs

           (B) TYPE: nucleic acid

           (C) STRANDEDNESS: single

           (D) TOPOLOGY: linear

20

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

25   CTGGTTCCTC CCAATGTG   18

    (2) INFORMATION FOR SEQ ID NO: 38:

30   (i) SEQUENCE CHARACTERISTICS:

           (A) LENGTH: 20 base pairs

           (B) TYPE: nucleic acid

           (C) STRANDEDNESS: single

           (D) TOPOLOGY: linear

35

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:

40   CCTCTCACTC CCCTCATCTC   20

    (2) INFORMATION FOR SEQ ID NO: 39:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 22 base pairs
        (B) TYPE: nucleic acid
5   (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

10   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

AAGCCAACCT TCCCTGCTTC TC   22

15 (2) INFORMATION FOR SEQ ID NO: 40:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 18 base pairs
            (B) TYPE: nucleic acid
20   (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: DNA

25   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 40:

CTGGTTCCTC CCAATGTG   18

30 (2) INFORMATION FOR SEQ ID NO: 41:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 20 base pairs
            (B) TYPE: nucleic acid
35   (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: DNA

40   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

GACGCTTATC GAGCAGCTTC   20

(2) INFORMATION FOR SEQ ID NO: 42:

     (i) SEQUENCE CHARACTERISTICS:

          (A) LENGTH: 24 base pairs

          (B) TYPE: nucleic acid

          (C) STRANDEDNESS: single

          (D) TOPOLOGY: linear

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

CTACCGCGCA ATGAACTCCT CGTC   24

(2) INFORMATION FOR SEQ ID NO: 43:

     (i) SEQUENCE CHARACTERISTICS:

          (A) LENGTH: 24 base pairs

          (B) TYPE: nucleic acid

          (C) STRANDEDNESS: single

          (D) TOPOLOGY: linear

     (ii) MOLECULE TYPE: DNA

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

CCTTCTTCTC CTCCTTCTTA GTGA   24

(2) INFORMATION FOR SEQ ID NO: 44:

     (i) SEQUENCE CHARACTERISTICS:

          (A) LENGTH: 2883 base pairs

          (B) TYPE: nucleic acid

          (C) STRANDEDNESS: single

          (D) TOPOLOGY: linear

     (ii) MOLECULE TYPE: cDNA to mRNA

     (iii) HYPOTHETICAL: NO

        (iv) ANTI-SENSE: NO

        (vi) ORIGINAL SOURCE:
             (A) ORGANISM: Rattus norwegicus

        (ix) FEATURE:
             (A) NAME/KEY: CDS
             (B) LOCATION:1..2883

        (x) PUBLICATION INFORMATION:
             (A) AUTHORS: Kaupmann, K
                          Huggel, K
                          Heid, J
                          Flor, P
                          Bischoff, S
                          Mickel, S
                          McMaster, G
                          Angst, C
                          Bittiger, H
                          Froestl, W
             (B) TITLE: Expression cloning of GABA-B receptors
                 uncovers similarity to metabotropic glutamate
                 receptors
             (C) JOURNAL: Nature
             (D) VOLUME: 386
             (F) PAGES: 239-246
             (G) DATE: 20 march-1997

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

    ATG CTG CTG CTG CTG CTG GTG CCT CTC TTC CTC CGC CCC CTG GGC GCT   48
    Met Leu Leu Leu Leu Leu Val Pro Leu Phe Leu Arg Pro Leu Gly Ala
     1   5   10   15

    GGC GGG GCG CAG ACC CCC AAC GCC ACC TCG GAA GGT TGC CAG ATT ATA   96
    Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile Ile
                20   25   30

    CAT CCG CCC TGG GAA GGT GGC ATC AGG TAC CGT GGC TTG ACT CGC GAC   144
    His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg Asp
                35   40   45

    CAG GTG AAG GCC ATC AAC TTC CTG CCT GTG GAC TAT GAG ATC GAA TAT   192

```
     Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu Tyr        —
         50              55              60

 5   GTG TGC CGA GGG GAG CGC GAG GTG GTG GGG CCC AAG GTG CGC AAA TGC        240
     Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys Cys
         65              70              75              80

10   CTG GCC AAC GGC TCC TGG ACG GAT ATG GAC ACA CCC AGC CGC TGT GTC        288
     Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys Val
                     85              90              95

     CGA ATC TGC TCC AAG TCT TAT TTG ACC CTG GAA AAT GGG AAG GTT TTC        336
     Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val Phe
                     100             105             110

15   CTG ACG GGT GGG GAC CTC CCA GCT CTG GAT GGA GCC CGG GTG GAG TTC        384
     Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Glu Phe
             115             120             125

20   CGA TGT GAC CCC GAC TTC CAT CTG GTG GGC AGC TCC CGG AGC GTC TGT        432
     Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Val Cys
             130             135             140

     AGT CAG GGC CAG TGG AGC ACC CCC AAG CCC CAC TGC CAG GTG AAT CGA        480
25   Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn Arg
     145             150             155             160

     ACG CCA CAC TCA GAA CGG CGT GCA GTA TAC ATC GGG GCG CTG TTT CCC        528
     Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro
                     165             170             175
30

     ATG AGC GGG GGC TGG CCG GGG GGC CAG GCC TGC CAG CCC GCG GTG GAG        576
     Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu
                     180             185             190
35

     ATG GCG CTG GAG GAC GTT AAC AGC CGC AGA GAC ATC CTG CCG GAC TAC        624
     Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr
                 195             200             205

40   GAG CTC AAG CTT ATC CAC CAC GAC AGC AAG TGT GAC CCA GGG CAA GCC        672
     Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala
             210             215             220
```

SUBSTITUTE SHEET (RULE 26)

```
ACC AAG TAC TTG TAC GAA CTA CTC TAC AAT GAC CCC ATC AAG ATC ATT        720
Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile
225                 230             235             240

CTC ATG CCT GGC TGT AGT TCT GTC TCC ACA CTT GTA GCT GAG GCT GCC        768
Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala
                245             250             255

CGG ATG TGG AAC CTT ATT GTG CTC TCA TAT GGC TCC AGT TCA CCA GCC        816
Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala
                260             265             270

TTG TCA AAC CGA CAG CGG TTT CCC ACG TTC TTC CGG ACG CAT CCA TCC        864
Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser
                275             280             285

GCC ACA CTC CAC AAT CCC ACC CGG GTG AAA CTC TTC GAA AAG TGG GGC        912
Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly
                290             295             300

TGG AAG AAG ATC GCT ACC ATC CAA CAG ACC ACC GAG GTC TTC ACC TCA        960
Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser
305                 310             315             320

ACG CTG GAT GAC CTG GAG GAG CGA GTG AAA GAG GCT GGG ATC GAG ATC       1008
Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile
                325             330             335

ACT TTC CGA CAG AGT TTC TTC TCG GAT CCA GCT GTG CCT GTT AAA AAC       1056
Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn
                340             345             350

CTG AAG CGT CAA GAT GCT CGA ATC ATC GTG GGA CTT TTC TAT GAG ACG       1104
Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr
                355             360             365

GAA GCC CGG AAA GTT TTT TGT GAG GTC TAT AAG GAA AGG CTC TTT GGG       1152
Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly
                370             375             380

AAG AAG TAC GTC TGG TTC CTC ATC GGG TGG TAT GCT GAC AAC TGG TTC       1200
Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe
385                 390             395             400
```

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AAG ACC TAT GAC CCG TCA ATC AAT TGT ACA GTG GAA GAA ATG ACC GAG   1248
Lys Thr Tyr Asp Pro Ser Ile Asn Cys Thr Val Glu Glu Met Thr Glu
            405   410   415

GCG GTG GAG GGC CAC ATC ACC ACG GAG ATT GTC ATG CTG AAC CCT GCC   1296
Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala
            420   425   430

AAC ACC CGA AGC ATT TCC AAC ATG ACG TCA CAG GAA TTT GTG GAG AAA   1344
Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys
            435   440   445

CTA ACC AAG CGG CTG AAA AGA CAC CCC GAG GAG ACT GGA GGC TTC CAG   1392
Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln
            450   455   460

GAG GCA CCA CTG GCC TAT GAT GCT ATC TGG GCC TTG GCT TTG GCC TTG   1440
Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu
465   470   475   480

AAC AAG ACG TCT GGA GGA GGT GGT CGT TCC GGC GTG CGC CTG GAG GAC   1488
Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp
            485   490   495

TTT AAC TAC AAC AAC CAG ACC ATT ACA GAC CAG ATC TAC CGG GCC ATG   1536
Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met
            500   505   510

AAC TCC TCC TCC TTT GAG GGC GTT TCT GGC CAT GTG GTC TTT GAT GCC   1584
Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala
            515   520   525

AGC GGC TCC CGG ATG GCA TGG ACA CTT ATC GAG CAG CTA CAG GGC GGC   1632
Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly
            530   535   540

AGC TAC AAG AAG ATC GGC TAC TAC GAC AGC ACC AAG GAT GAT CTT TCC   1680
Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser
545   550   555   560

TGG TCC AAA ACG GAC AAG TGG ATT GGA GGG TCT CCC CCA GCT GAC CAG   1728
Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln

---

H1865-1 WO SEQ   20

565   570   575

```
ACC TTG GTC ATC AAG ACA TTC CGT TTC CTG TCT CAG AAA CTC TTT ATC      1776
Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile
        580                 585                 590
```

```
TCC GTC TCA GTT CTC TCC AGC CTG GGC ATT GTT CTT GCT GTT GTC TGT      1824
Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys
        595                 600                 605
```

```
CTG TCC TTT AAC ATC TAC AAC TCC CAC GTT CGT TAT ATC CAG AAC TCC      1872
Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser
        610                 615                 620
```

```
CAG CCC AAC CTG AAC AAT CTG ACT GCT GTG GGC TGC TCA CTG GCA CTG      1920
Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu
625                 630                 635                 640
```

```
GCT GCT GTC TTC CCT CTC GGG CTG GAT GGT TAC CAC ATA GGG AGA AGC      1968
Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Ser
                645                 650                 655
```

```
CAG TTC CCG TTT GTC TGC CAG GCC CGC CTT TGG CTC TTG GGC TTG GGC      2016
Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly
                660                 665                 670
```

```
TTT AGT CTG GGC TAT GGC TCT ATG TTC ACC AAG ATC TGG TGG GTC CAC      2064
Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His
                675                 680                 685
```

```
ACA GTC TTC ACG AAG AAG GAG GAG AAG AAG GAG TGG AGG AAG ACC CTA      2112
Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu
        690                 695                 700
```

```
GAG CCC TGG AAA CTC TAT GCC ACT GTG GGC CTG CTG GTG GGC ATG GAT      2160
Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp
705                 710                 715                 720
```

```
GTC CTG ACT CTT GCC ATC TGG CAG ATT GTG GAC CCC TTG CAC CGA ACC      2208
Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr
                725                 730                 735
```

```
ATT GAG ACT TTT GCC AAG GAG GAA CCA AAG GAA GAC ATC GAT GTC TCC      2256
```

H1865-1 WO SEQ   21

```
     Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser        —
             740                 745                 750


     ATT CTG CCC CAG TTG GAG CAC TGC AGC TCC AAG AAG ATG AAT ACG TGG        2304
 5   Ile Leu Pro Gln Leu Glu His Cys Ser Ser Lys Lys Met Asn Thr Trp
             755                 760                 765


     CTT GGC ATT TTC TAT GGT TAC AAG GGG CTG CTG CTG CTG CTG GGA ATC        2352
10   Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile
             770                 775                 780


     TTT CTT GCT TAC GAA ACC AAG AGC GTG TCC ACT GAA AAG ATC AAT GAC        2400
     Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp
     785                 790                 795                 800

15
     CAC AGG GCC GTG GGC ATG GCT ATC TAC AAT GTC GCG GTC CTG TGT CTC        2448
     His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu
                 805                 810                 815


20   ATC ACT GCT CCT GTG ACC ATG ATC CTT TCC AGT CAG CAG GAC GCA GCC        2496
     Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala
                 820                 825                 830


     TTT GCC TTT GCC TCT CTG GCC ATC GTG TTC TCT TCC TAC ATC ACT CTG        2544
25   Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu
                 835                 840                 845


     GTT GTG CTC TTT GTG CCC AAG ATG CGC AGG CTG ATC ACC CGA GGG GAA        2592
     Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu
30           850                 855                 860


     TGG CAG TCT GAA ACG CAG GAC ACC ATG AAA ACA GGA TCA TCC ACC AAC        2640
     Trp Gln Ser Glu Thr Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn
     865                 870                 875                 880

35
     AAC AAC GAG GAA GAG AAG TCC CGA CTG TTG GAG AAG GAA AAC CGA GAA        2688
     Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu
                 885                 890                 895


40   CTG GAA AAG ATC ATC GCT GAG AAA GAG GAG CGC GTC TCT GAA CTG CGC        2736
     Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg
                 900                 905                 910
```

```
CAT CAG CTC CAG TCT CGG CAG CAA CTC CGC TCA CGG CGC CAC CCC CCA    2784
His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro
        915             920             925

ACA CCC CCA GAT CCC TCT GGG GGC CTT CCC AGG GGA CCC TCT GAG CCC    2832
Thr Pro Pro Asp Pro Ser Gly Gly Leu Pro Arg Gly Pro Ser Glu Pro
        930             935             940

CCT GAC CGG CTT AGC TGT GAT GGG AGT CGA GTA CAT TTG CTT TAC AAG    2880
Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys
945             950             955             960

TGA                                                               2883
 *
```

(2) INFORMATION FOR SEQ ID NO: 45:

  (i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 960 amino acids
    (B) TYPE: amino acid
    (D) TOPOLOGY: linear

  (ii) MOLECULE TYPE: protein

  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:

```
Met Leu Leu Leu Leu Leu Val Pro Leu Phe Leu Arg Pro Leu Gly Ala
1               5               10              15

Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile Ile
            20              25              30

His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg Asp
        35              40              45

Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu Tyr
        50              55              60

Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys Cys
65              70              75              80

Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys Val
```

```
                      85                    90                    95

       Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val Phe
                   100                   105                   110

  5    Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Glu Phe
                   115                   120                   125

       Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Val Cys
  10             130                   135                   140

       Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn Arg
       145                   150                   155                   160

  15   Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro
                         165                   170                   175

       Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu
                   180                   185                   190

  20   Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr
                   195                   200                   205

       Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala
  25             210                   215                   220

       Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile
       225                   230                   235                   240

  30   Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala
                         245                   250                   255

       Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala
                   260                   265                   270

  35   Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser
                   275                   280                   285

       Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly
  40             290                   295                   300

       Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser
       305                   310                   315                   320
```

SUBSTITUTE SHEET (RULE 26)

Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile
                325   330   335

5   Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn
                340   345   350

    Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr
                355   360   365
10
    Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly
        370   375   380

    Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe
15 385   390   395   400

    Lys Thr Tyr Asp Pro Ser Ile Asn Cys Thr Val Glu Glu Met Thr Glu
                405   410   415

20 Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala
                420   425   430

    Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys
                435   440   445
25
    Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln
        450   455   460

    Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu
30 465   470   475   480

    Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp
                485   490   495

35 Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met
                500   505   510

    Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala
                515   520   525
40
    Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly
        530   535   540

H1865-1 WO SEQ   25

```
   Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser
   545             550             555             560


   Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln
5                  565             570             575


   Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile
                   580             585             590


10 Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys
                   595             600             605


   Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser
       610             615             620

15
   Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu
   625             630             635             640


   Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Ser
20                 645             650             655


   Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly
                   660             665             670


25 Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His
       675             680             685


   Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu
       690             695             700

30
   Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp
   705             710             715             720


   Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr
35                 725             730             735


   Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser
                   740             745             750


40 Ile Leu Pro Gln Leu Glu His Cys Ser Ser Lys Lys Met Asn Thr Trp
       755             760             765


   Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile
```

SUBSTITUTE SHEET (RULE 26)

                770   775   780

Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp
785   790   795   800

His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu
                805   810   815

Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala
                820   825   830

Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu
                835   840   845

Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu
                850   855   860

Trp Gln Ser Glu Thr Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn
865   870   875   880

Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu
                885   890   895

Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg
                900   905   910

His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro
                915   920   925

Thr Pro Pro Asp Pro Ser Gly Gly Leu Pro Arg Gly Pro Ser Glu Pro
                930   935   940

Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys
945   950   955   960

(2) INFORMATION FOR SEQ ID NO: 46:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 2538 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
　　　　　(A) ORGANISM: Rattus norwegicus

(ix) FEATURE:
　　　　　(A) NAME/KEY: CDS
　　　　　(B) LOCATION:1..2532

(x) PUBLICATION INFORMATION:
　　　　　(A) AUTHORS: Kaupmann, K
　　　　　　　　　　　　Huggel, K
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　　　　　　　　　　　　Flor, P
　　　　　　　　　　　　Bischoff, M
　　　　　　　　　　　　Mickel, S
　　　　　　　　　　　　McMaster, G
　　　　　　　　　　　　Angst, C
　　　　　　　　　　　　Bittiger, H
　　　　　　　　　　　　Froestl, W
　　　　　(B) TITLE: Expression cloning of GABA-B receptors
　　　　　　　　　uncovers similarity to metabotropic glutamate
　　　　　　　　　receptors
　　　　　(C) JOURNAL: Nature
　　　　　(D) VOLUME: 386
　　　　　(F) PAGES: 239-246
　　　　　(G) DATE: 20 March-1997

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

```
ATG GGC CCG GGG GGA CCC TGT ACC CCA GTG GGG TGG CCG CTG CCT CTT        48
Met Gly Pro Gly Gly Pro Cys Thr Pro Val Gly Trp Pro Leu Pro Leu
 1               5                  10                  15


CTG CTG GTG ATG GCG GCT GGG GTG GCT CCG GTG TGG GCC TCT CAC TCC        96
Leu Leu Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
             20                  25                  30
```

```
    CCT CAT CTC CCG CGG CCT CAC CCG AGG GTC CCC CCG CAC CCC TCC TCA    144
    Pro His Leu Pro Arg Pro His Pro Arg Val Pro Pro His Pro Ser Ser
            35                  40                  45
```

```
5   GAA CGG CGT GCA GTA TAC ATC GGG GCG CTG TTT CCC ATG AGC GGG GGC    192
    Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
            50                  55                  60
```

```
    TGG CCG GGG GGC CAG GCC TGC CAG CCC GCG GTG GAG ATG GCG CTG GAG    240
10  Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
        65                  70                  75                  80
```

```
    GAC GTT AAC AGC CGC AGA GAC ATC CTG CCG GAC TAC GAG CTC AAG CTT    288
    Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
15                  85                  90                  95
```

```
    ATC CAC CAC GAC AGC AAG TGT GAC CCA GGG CAA GCC ACC AAG TAC TTG    336
    Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
                    100                 105                 110
20
    TAC GAA CTA CTC TAC AAT GAC CCC ATC AAG ATC ATT CTC ATG CCT GGC    384
    Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
            115                 120                 125
```

```
25  TGT AGT TCT GTC TCC ACA CTT GTA GCT GAG GCT GCC CGG ATG TGG AAC    432
    Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
            130                 135                 140
```

```
    CTT ATT GTG CTC TCA TAT GGC TCC AGT TCA CCA GCC TTG TCA AAC CGA    480
30  Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
    145                 150                 155                 160
```

```
    CAG CGG TTT CCC ACG TTC TTC CGG ACG CAT CCA TCC GCC ACA CTC CAC    528
    Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
35                  165                 170                 175
```

```
    AAT CCC ACC CGG GTG AAA CTC TTC GAA AAG TGG GGC TGG AAG AAG ATC    576
    Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
                    180                 185                 190
40                                                                  ᴅ
    GCT ACC ATC CAA CAG ACC ACC GAG GTC TTC ACC TCA ACG CTG GAT GAC    624
    Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
                    195                 200                 205
```

SUBSTITUTE SHEET (RULE 26)

CTG GAG GAG CGA GTG AAA GAG GCT GGG ATC GAG ATC ACT TTC CGA CAG   672
Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
    210   215   220

AGT TTC TTC TCG GAT CCA GCT GTG CCT GTT AAA AAC CTG AAG CGT CAA   720
Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
225   230   235   240

GAT GCT CGA ATC ATC GTG GGA CTT TTC TAT GAG ACG GAA GCC CGG AAA   768
Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
                245   250   255

GTT TTT TGT GAG GTC TAT AAG GAA AGG CTC TTT GGG AAG AAG TAC GTC   816
Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
                260   265   270

TGG TTC CTC ATC GGG TGG TAT GCT GAC AAC TGG TTC AAG ACC TAT GAC   864
Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Thr Tyr Asp
        275   280   285

CCG TCA ATC AAT TGT ACA GTG GAA GAA ATG ACC GAG GCG GTG GAG GGC   912
Pro Ser Ile Asn Cys Thr Val Glu Glu Met Thr Glu Ala Val Glu Gly
    290   295   300

CAC ATC ACC ACG GAG ATT GTC ATG CTG AAC CCT GCC AAC ACC CGA AGC   960
His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
305   310   315   320

ATT TCC AAC ATG ACG TCA CAG GAA TTT GTG GAG AAA CTA ACC AAG CGG   1008
Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
                325   330   335

CTG AAA AGA CAC CCC GAG GAG ACT GGA GGC TTC CAG GAG GCA CCA CTG   1056
Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
                340   345   350

GCC TAT GAT GCT ATC TGG GCC TTG GCT TTG GCC TTG AAC AAG ACG TCT   1104
Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
                355   360   365

GGA GGA GGT GGT CGT TCC GGC GTG CGC CTG GAG GAC TTT AAC TAC AAC   1152
Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn

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H1865-1 WO SEQ   30

```
        370                    375                    380

    AAC CAG ACC ATT ACA GAC CAG ATC TAC CGG GCC ATG AAC TCC TCC TCC      1200
    Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
5   385                    390                    395              400


    TTT GAG GGC GTT TCT GGC CAT GTG GTC TTT GAT GCC AGC GGC TCC CGG      1248
    Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
                        405                    410              415
10
    ATG GCA TGG ACA CTT ATC GAG CAG CTA CAG GGC GGC AGC TAC AAG AAG      1296
    Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
                    420                    425              430


15  ATC GGC TAC TAC GAC AGC ACC AAG GAT GAT CTT TCC TGG TCC AAA ACG      1344
    Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                435                    440              445


    GAC AAG TGG ATT GGA GGG TCT CCC CCA GCT GAC CAG ACC TTG GTC ATC      1392
20  Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile
            450                    455              460


    AAG ACA TTC CGT TTC CTG TCT CAG AAA CTC TTT ATC TCC GTC TCA GTT      1440
    Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile Ser Val Ser Val
25  465                    470                    475              480


    CTC TCC AGC CTG GGC ATT GTT CTT GCT GTT GTC TGT CTG TCC TTT AAC      1488
    Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn
                    485                    490              495
30
    ATC TAC AAC TCC CAC GTT CGT TAT ATC CAG AAC TCC CAG CCC AAC CTG      1536
    Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu
                500                    505              510


35  AAC AAT CTG ACT GCT GTG GGC TGC TCA CTG GCA CTG GCT GCT GTC TTC      1584
    Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu Ala Ala Val Phe
                515                    520              525


    CCT CTC GGG CTG GAT GGT TAC CAC ATA GGG AGA AGC CAG TTC CCG TTT      1632
40  Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Ser Gln Phe Pro Phe     ʋ
                530                    535              540


    GTC TGC CAG GCC CGC CTT TGG CTC TTG GGC TTG GGC TTT AGT CTG GGC      1680
```

H1865-1 WO SEQ   31

```
            Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly          —
            545             550             555             560


            TAT GGC TCT ATG TTC ACC AAG ATC TGG TGG GTC CAC ACA GTC TTC ACG      1728
 5          Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His Thr Val Phe Thr
                                565             570             575


            AAG AAG GAG GAG AAG AAG GAG TGG AGG AAG ACC CTA GAG CCC TGG AAA      1776
            Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys
10                          580             585             590


            CTC TAT GCC ACT GTG GGC CTG CTG GTG GGC ATG GAT GTC CTG ACT CTT      1824
            Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp Val Leu Thr Leu
                        595             600             605

15
            GCC ATC TGG CAG ATT GTG GAC CCC TTG CAC CGA ACC ATT GAG ACT TTT      1872
            Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr Ile Glu Thr Phe
                    610             615             620


20          GCC AAG GAG GAA CCA AAG GAA GAC ATC GAT GTC TCC ATT CTG CCC CAG      1920
            Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser Ile Leu Pro Gln
            625             630             635             640


            TTG GAG CAC TGC AGC TCC AAG AAG ATG AAT ACG TGG CTT GGC ATT TTC      1968
25          Leu Glu His Cys Ser Ser Lys Lys Met Asn Thr Trp Leu Gly Ile Phe
                            645             650             655


            TAT GGT TAC AAG GGG CTG CTG CTG CTG CTG GGA ATC TTT CTT GCT TAC      2016
            Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr
30                      660             665             670


            GAA ACC AAG AGC GTG TCC ACT GAA AAG ATC AAT GAC CAC AGG GCC GTG      2064
            Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp His Arg Ala Val
                        675             680             685

35
            GGC ATG GCT ATC TAC AAT GTC GCG GTC CTG TGT CTC ATC ACT GCT CCT      2112
            Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu Ile Thr Ala Pro
                    690             695             700


40          GTG ACC ATG ATC CTT TCC AGT CAG CAG GAC GCA GCC TTT GCC TTT GCC      2160
            Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala
            705             710             715             720
```

```
    TCT CTG GCC ATC GTG TTC TCT TCC TAC ATC ACT CTG GTT GTG CTC TTT    2208
    Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu Val Val Leu Phe
                    725                 730                 735

 5  GTG CCC AAG ATG CGC AGG CTG ATC ACC CGA GGG GAA TGG CAG TCT GAA    2256
    Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu
                    740                 745                 750

    ACG CAG GAC ACC ATG AAA ACA GGA TCA TCC ACC AAC AAC AAC GAG GAA    2304
10  Thr Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu
                    755                 760                 765

    GAG AAG TCC CGA CTG TTG GAG AAG GAA AAC CGA GAA CTG GAA AAG ATC    2352
    Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile
15       770                 775                 780

    ATC GCT GAG AAA GAG GAG CGC GTC TCT GAA CTG CGC CAT CAG CTC CAG    2400
    Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln
    785                 790                 795                 800
20
    TCT CGG CAG CAA CTC CGC TCA CGG CGC CAC CCC CCA ACA CCC CCA GAT    2448
    Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Asp
                    805                 810                 815

25  CCC TCT GGG GGC CTT CCC AGG GGA CCC TCT GAG CCC CCT GAC CGG CTT    2496
    Pro Ser Gly Gly Leu Pro Arg Gly Pro Ser Glu Pro Pro Asp Arg Leu
                    820                 825                 830

    AGC TGT GAT GGG AGT CGA GTA CAT TTG CTT TAC AAG TGA                2535
30  Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys  *
                    835                 840
```

(2) INFORMATION FOR SEQ ID NO: 47:

35
            (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 844 amino acids
                (B) TYPE: amino acid
                (D) TOPOLOGY: linear

40
        (ii) MOLECULE TYPE: protein

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:

```
        Met Gly Pro Gly Gly Pro Cys Thr Pro Val Gly Trp Pro Leu Pro Leu
         1               5                  10                  15

5       Leu Leu Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
                     20                  25                  30

        Pro His Leu Pro Arg Pro His Pro Arg Val Pro Pro His Pro Ser Ser
                     35                  40                  45
10
        Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
             50                  55                  60

        Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
15       65                  70                  75                  80

        Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
                         85                  90                  95

20      Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
                     100                 105                 110

        Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
             115                 120                 125
25
        Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
             130                 135                 140

        Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
30      145                 150                 155                 160

        Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
                     165                 170                 175

35      Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
                     180                 185                 190

        Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
                     195                 200                 205
40
        Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
             210                 215                 220
```

SUBSTITUTE SHEET (RULE 26)

```
Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
225             230             235             240


Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
                245             250             255


Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
                260             265             270


Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Thr Tyr Asp
                275             280             285


Pro Ser Ile Asn Cys Thr Val Glu Glu Met Thr Glu Ala Val Glu Gly
                290             295             300


His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
305             310             315             320


Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
                325             330             335


Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
                340             345             350


Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
                355             360             365


Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn
                370             375             380


Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
385             390             395             400


Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
                405             410             415


Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
                420             425             430


Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                435             440             445


Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile
```

SUBSTITUTE SHEET (RULE 26)

```
            450                    455                    460

    Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile Ser Val Ser Val
    465                    470                    475                    480

    Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn
                    485                    490                    495

    Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu
                    500                    505                    510

    Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu Ala Ala Val Phe
                    515                    520                    525

    Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Ser Gln Phe Pro Phe
                    530                    535                    540

    Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly
    545                    550                    555                    560

    Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His Thr Val Phe Thr
                    565                    570                    575

    Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys
                    580                    585                    590

    Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp Val Leu Thr Leu
                    595                    600                    605

    Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr Ile Glu Thr Phe
                    610                    615                    620

    Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser Ile Leu Pro Gln
    625                    630                    635                    640

    Leu Glu His Cys Ser Ser Lys Lys Met Asn Thr Trp Leu Gly Ile Phe
                    645                    650                    655

    Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr
                    660                    665                    670

    Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp His Arg Ala Val
                    675                    680                    685
```

SUBSTITUTE SHEET (RULE 26)

```
Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu Ile Thr Ala Pro
    690                 695             700

Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala
705·                710             715                 720

Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu Val Val Leu Phe
                725             730                 735

Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu
            740             745             750

Thr Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu
        755             760             765

Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile
    770             775             780

Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln
785             790             795                 800

Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Asp
            805             810             815

Pro Ser Gly Gly Leu Pro Arg Gly Pro Ser Glu Pro Pro Asp Arg Leu
        820             825             830

Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys
    835             840
```

(2). INFORMATION FOR SEQ ID NO: 48:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 2886 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA to mRNA

    (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
        (A) ORGANISM: Homo sapiens

(ix) FEATURE:
        (A) NAME/KEY: CDS
        (B) LOCATION:1..2886

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:

```
ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC        48
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
1               5                  10                  15

GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC        96
Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
            20                  25                  30

ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG       144
Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35                  40                  45

GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG       192
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
        50                  55                  60

TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG       240
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
65                  70                  75                  80

TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT       288
Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                85                  90                  95

GTC CGA ATC TGC TCC AAG TCT TAT TTG ACC CTG GAA AAT GGG AAG GTT       336
Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
            100                 105                 110

TTC CTG ACG GGT GGG GAC CTC CCA GCT CTG GAC GGA GCC CGG GTG GAT       384
Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
            115                 120                 125
```

TTC CGG TGT GAC CCC GAC TTC CAT CTG GTG GGC AGC TCC CGG AGC ATC 432
Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile
130   135   140

TGT AGT CAG GGC CAG TGG AGC ACC CCC AAG CCC CAC TGC CAG GTG AAT 480
Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn
145   150   155   160

CGA ACG CCA CAC TCA GAA CGG CGC GCA GTG TAC ATC GGG GCA CTG TTT 528
Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe
              165   170   175

CCC ATG AGC GGG GGC TGG CCA GGG GGC CAG GCC TGC CAG CCC GCG GTG' 576
Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val
              180   185   190

GAG ATG GCG CTG GAG GAC GTG AAT AGC CGC AGG GAC ATC CTG CCG GAC 624
Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp
              195   200   205

TAT GAG CTC AAG CTC ATC CAC CAC GAC AGC AAG TGT GAT CCA GGC CAA 672
Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln
              210   215   220

GCC ACC AAG TAC CTA TAT GAG CTG CTC TAC AAC GAC CCT ATC AAG ATC 720
Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile
225   230   235   240

ATC CTT ATG CCT GGC TGC AGC TCT GTC TCC ACG CTG GTG GCT GAG GCT 768
Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala
              245   250   255

GCT AGG ATG TGG AAC CTC ATT GTG CTT TCC TAT GGC TCC AGC TCA CCA 816
Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro
              260   265   270

GCC CTG TCA AAC CGG CAG CGT TTC CCC ACT TTC TTC CGA ACG CAC CCA 864
Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro
              275   280   285   ʋ

TCA GCC ACA CTC CAC AAC CCT ACC CGC GTG AAA CTC TTT GAA AAG TGG 912
Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp

| | 290 | 295 | 300 | |

```
        GGC TGG AAG AAG ATT GCT ACC ATC CAG CAG ACC ACT GAG GTC TTC ACT        960
        Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr
 5      305              310              315              320


        TCG ACT CTG GAC GAC CTG GAG GAA CGA GTG AAG GAG GCT GGA ATT GAG       1008
        Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu
                         325              330              335
10
        ATT ACT TTC CGC CAG AGT TTC TTC TCA GAT CCA GCT GTG CCC GTC AAA       1056
        Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys
                         340              345              350


15      AAC CTG AAG CGC CAG GAT GCC CGA ATC ATC GTG GGA CTT TTC TAT GAG       1104
        Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu
                         355              360              365


        ACT GAA GCC CGG AAA GTT TTT TGT GAG GTG TAC AAG GAG CGT CTC TTT       1152
20      Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe
                 370              375              380


        GGG AAG AAG TAC GTC TGG TTC CTC ATT GGG TGG TAT GCT GAC AAT TGG       1200
        Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp
25      385              390              395              400


        TTC AAG ATC TAC GAC CCT TCT ATC AAC TGC ACA GTG GAT GAG ATG ACT       1248
        Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr
                         405              410              415
30
        GAG GCG GTG GAG GGC CAC ATC ACA ACT GAG ATT GTC ATG CTG AAT CCT       1296
        Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro
                         420              425              430


35      GCC AAT ACC CGC AGC ATT TCC AAC ATG ACA TCC CAG GAA TTT GTG GAG       1344
        Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu
                         435              440              445


        AAA CTA ACC AAG CGA CTG AAA AGA CAC CCT GAG GAG ACA GGA GGC TTC       1392
40      Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe
                         450              455              460


        CAG GAG GCA CCG CTG GCC TAT GAT GCC ATC TGG GCC TTG GCA CTG GCC       1440
```

H1865-1 WO SEQ   40

```
     Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala
     465             470             475             480


     CTG AAC AAG ACA TCT GGA GGA GGC GGC CGT TCT GGT GTG CGC CTG GAG       1488
  5  Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu
                     485             490             495


     GAC TTC AAC TAC AAC AAC CAG ACC ATT ACC GAC CAA ATC TAC CGG GCA       1536
     Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala
 10                  500             505             510


     ATG AAC TCT TCG TCC TTT GAG GGT GTC TCT GGC CAT GTG GTG TTT GAT       1584
     Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp
                     515             520             525
 15

     GCC AGC GGC TCT CGG ATG GCA TGG ACG CTT ATC GAG CAG CTT CAG GGT       1632
     Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly
             530             535             540


 20  GGC AGC TAC AAG AAG ATT GGC TAC TAT GAC AGC ACC AAG GAT GAT CTT       1680
     Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu
     545             550             555             560


     TCC TGG TCC AAA ACA GAT AAA TGG ATT GGA GGG TCC CCC CCA GCT GAC       1728
 25  Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp
                     565             570             575


     CAG ACC CTG GTC ATC AAG ACA TTC CGC TTC CTG TCA CAG AAA CTC TTT       1776
     Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe
 30                  580             585             590


     ATC TCC GTC TCA GTT CTC TCC AGC CTG GGC ATT GTC CTA GCT GTT GTC       1824
     Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val
                     595             600             605
 35

     TGT CTG TCC TTT AAC ATC TAC AAC TCA CAT GTC CGT TAT ATC CAG AAC       1872
     Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn
             610             615             620


 40  TCA CAG CCC AAC CTG AAC AAC CTG ACT GCT GTG GGC TGC TCA CTG GCT       1920
     Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala
     625             630             635             640
```

TTA GCT GCT GTC TTC CCC CTG GGG CTC GAT GGT TAC CAC ATT GGG AGG   1968
Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg
            645   650   655

AAC CAG TTT CCT TTC GTC TGC CAG GCC CGC CTC TGG CTC CTG GGC CTG   2016
Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu
            660   665   670

GGC TTT AGT CTG GGC TAC GGT TCC ATG TTC ACC AAG ATT TGG TGG GTC   2064
Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val
            675   680   685

CAC ACG GTC TTC ACA AAG AAG GAA GAA AAG AAG GAG TGG AGG AAG ACT   2112
His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr
        690   695   700

CTG GAA CCC TGG AAG CTG TAT GCC ACA GTG GGC CTG CTG GTG GGC ATG   2160
Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met
705   710   715   720

GAT GTC CTC ACT CTC GCC ATC TGG CAG ATC GTG GAC CCT CTG CAC CGG   2208
Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg
            725   730   735

ACC ATT GAG ACA TTT GCC AAG GAG GAA CCT AAG GAA GAT ATT GAC GTC   2256
Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val
            740   745   750

TCT ATT CTG CCC CAG CTG GAG CAT TGC AGC TCC AGG AAG ATG AAT ACA   2304
Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met Asn Thr
            755   760   765

TGG CTT GGC ATT TTC TAT GGT TAC AAG GGG CTG CTG CTG CTG CTG GGA   2352
Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly
        770   775   780

ATC TTC CTT GCT TAT GAG ACC AAG AGT GTG TCC ACT GAG AAG ATC AAT   2400
Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn
785   790   795   800

GAT CAC CGG GCT GTG GGC ATG GCT ATC TAC AAT GTG GCA GTC CTG TGC   2448
Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys
            805   810   815

H1865-1 WO SEQ   42

CTC ATC ACT GCT CCT GTC ACC ATG ATT CTG TCC AGC CAG CAG GAT GCA   2496
Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala
            820   825   830

GCC TTT GCC TTT GCC TCT CTT GCC ATA GTT TTC TCC TCC TAT ATC ACT   2544
Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr
            835   840   845

CTT GTT GTG CTC TTT GTG CCC AAG ATG CGC AGG CTG ATC ACC CGA GGG   2592
Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly
        850   855   860

GAA TGG CAG TCG GAG GCG CAG GAC ACC ATG AAG ACA GGG TCA TCG ACC   2640
Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly Ser Ser Thr
865   870   875   880

AAC AAC AAC GAG GAG GAG AAG TCC CGG CTG TTG GAG AAG GAG AAC CGT   2688
Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg
                885   890   895

GAA CTG GAA AAG ATC ATT GCT GAG AAA GAG GAG CGT GTC TCT GAA CTG   2736
Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu
            900   905   910

CGC CAT CAA CTC CAG TCT CGG CAG CAG CTC CGC TCC CGG CGC CAC CCA   2784
Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro
            915   920   925

CCG ACA CCC CCA GAA CCC TCT GGG GGC CTG CCC AGG GGA CCC CCT GAG   2832
Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro Arg Gly Pro Pro Glu
            930   935   940

CCC CCC GAC CGG CTT AGC TGT GAT GGG AGT CGA GTG CAT TTG CTT TAT   2880
Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr
945   950   955   960

AAG TGA   2886
Lys *

(2) INFORMATION FOR SEQ ID NO: 49:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 961 amino acids
            (B) TYPE: amino acid
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 49:

Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1   5   10   15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
             20   25   30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
             35   40   45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
         50   55   60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65   70   75   80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                 85   90   95

Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
             100   105   110

Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
             115   120   125

Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile
         130   135   140

Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn
145   150   155   160

Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe
                 165   170   175

```
        Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val
                    180             185             190


        Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp
    5           195             200             205


        Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln
                210             215             220


    10  Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile
        225             230             235             240


        Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala
                    245             250             255
    15
        Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro
                    260             265             270


        Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro
    20          275             280             285


        Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp
                290             295             300


    25  Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr
        305             310             315             320


        Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu
                    325             330             335
    30
        Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys
                    340             345             350


        Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu
    35          355             360             365


        Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe
                370             375             380


    40  Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp
        385             390             395             400


        Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr
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SUBSTITUTE SHEET (RULE 26)

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                     405                    410                    415
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Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro
              420   425   430

Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu
              435   440   445

Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe
    450   455   460

Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala
465   470   475   480

Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu
                  485   490   495

Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala
              500   505   510

Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp
              515   520   525

Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly
    530   535   540

Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu
545   550   555   560

Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp
                  565   570   575

Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe
              580   585   590

Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val
              595   600   605

Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn
    610   615   620

Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala
625   630   635   640

```
    Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg
                    645             650             655

 5  Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu
                    660             665             670

    Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val
                    675             680             685
10
    His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr
                690             695             700

    Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met
15  705             710             715             720

    Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg
                    725             730             735

20  Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val
                    740             745             750

    Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met Asn Thr
                    755             760             765
25
    Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly
        770             775             780

    Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn
30  785             790             795             800

    Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys
                    805             810             815

35  Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala
                    820             825             830

    Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr
                    835             840             845
40
    Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly
                850             855             860
```

Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly Ser Ser Thr
865   870   875   880

Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg
                885   890   895

Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu
            900   905   910

Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro
        915   920   925

Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro Arg Gly Pro Pro Glu
    930   935   940

Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr
945   950   955   960

Lys

(2) INFORMATION FOR SEQ ID NO: 50:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 2535 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA to rRNA

        (iii) HYPOTHETICAL: NO

        (iv) ANTI-SENSE: NO

        (vi) ORIGINAL SOURCE:
            (A) ORGANISM: Homo sapiens

        (ix) FEATURE:
            (A) NAME/KEY: CDS
            (B) LOCATION:1..2535

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:

```
       ATG GGG CCC GGG GCC CCT TTT GCC CGG GTG GGG TGG CCA CTG CCG CTT          48
       Met Gly Pro Gly Ala Pro Phe Ala Arg Val Gly Trp Pro Leu Pro Leu
5       1               5                   10                  15


       CTG GTT GTG ATG GCG GCA GGG GTG GCT CCG GTG TGG GCC TCC CAC TCC          96
       Leu Val Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
                       20                  25                  30
10
       CCC CAT CTC CCG CGG CCT CAC TCG CGG GTC CCC CCG CAC CCC TCC TCA         144
       Pro His Leu Pro Arg Pro His Ser Arg Val Pro Pro His Pro Ser Ser
                   35                  40                  45

15     GAA CGG CGC GCA GTG TAC ATC GGG GCA CTG TTT CCC ATG AGC GGG GGC         192
       Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
           50                  55                  60


       TGG CCA GGG GGC CAG GCC TGC CAG CCC GCG GTG GAG ATG GCG CTG GAG         240
20     Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
       65                  70                  75                  80


       GAC GTG AAT AGC CGC AGG GAC ATC CTG CCG GAC TAT GAG CTC AAG CTC         288
       Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
25                          85                  90                  95


       ATC CAC CAC GAC AGC AAG TGT GAT CCA GGC CAA GCC ACC AAG TAC CTA         336
       Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
                       100                 105                 110
30
       TAT GAG CTG CTC TAC AAC GAC CCT ATC AAG ATC ATC CTT ATG CCT GGC         384
       Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
               115                 120                 125


35     TGC AGC TCT GTC TCC ACG CTG GTG GCT GAG GCT GCT AGG ATG TGG AAC         432
       Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
               130                 135                 140


       CTC ATT GTG CTT TCC TAT GGC TCC AGC TCA CCA GCC CTG TCA AAC CGG         480
40     Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
       145                 150                 155                 160


       CAG CGT TTC CCC ACT TTC TTC CGA ACG CAC CCA TCA GCC ACA CTC CAC         528
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      Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His      —
                  165             170             175

      AAC CCT ACC CGC GTG AAA CTC TTT GAA AAG TGG GGC TGG AAG AAG ATT      576
   5  Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
                  180             185             190

      GCT ACC ATC CAG CAG ACC ACT GAG GTC TTC ACT TCG ACT CTG GAC GAC      624
      Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
  10              195             200             205

      CTG GAG GAA CGA GTG AAG GAG GCT GGA ATT GAG ATT ACT TTC CGC CAG      672
      Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
                  210             215             220
  15
      AGT TTC TTC TCA GAT CCA GCT GTG CCC GTC AAA AAC CTG AAG CGC CAG      720
      Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
      225             230             235             240

  20  GAT GCC CGA ATC ATC GTG GGA CTT TTC TAT GAG ACT GAA GCC CGG AAA      768
      Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
                  245             250             255

      GTT TTT TGT GAG GTG TAC AAG GAG CGT CTC TTT GGG AAG AAG TAC GTC      816
  25  Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
                  260             265             270

      TGG TTC CTC ATT GGG TGG TAT GCT GAC AAT TGG TTC AAG ATC TAC GAC      864
      Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp
  30              275             280             285

      CCT TCT ATC AAC TGC ACA GTG GAT GAG ATG ACT GAG GCG GTG GAG GGC      912
      Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly
                  290             295             300
  35
      CAC ATC ACA ACT GAG ATT GTC ATG CTG AAT CCT GCC AAT ACC CGC AGC      960
      His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
      305             310             315             320

  40  ATT TCC AAC ATG ACA TCC CAG GAA TTT GTG GAG AAA CTA ACC AAG CGA      1008
      Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
                  325             330             335
```

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      CTG AAA AGA CAC CCT GAG GAG ACA GGA GGC TTC CAG GAG GCA CCG CTG        1056
      Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
                  340                 345                 350

  5   GCC TAT GAT GCC ATC TGG GCC TTG GCA CTG GCC CTG AAC AAG ACA TCT        1104
      Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
                  355                 360                 365

      GGA GGA GGC GGC CGT TCT GGT GTG CGC CTG GAG GAC TTC AAC TAC AAC        1152
 10   Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn
                  370                 375                 380

      AAC CAG ACC ATT ACC GAC CAA ATC TAC CGG GCA ATG AAC TCT TCG TCC        1200
      Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
 15   385                 390                 395                 400

      TTT GAG GGT GTC TCT GGC CAT GTG GTG TTT GAT GCC AGC GGC TCT CGG        1248
      Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
                  405                 410                 415
 20
      ATG GCA TGG ACG CTT ATC GAG CAG CTT CAG GGT GGC AGC TAC AAG AAG        1296
      Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
                  420                 425                 430

 25   ATT GGC TAC TAT GAC AGC ACC AAG GAT GAT CTT TCC TGG TCC AAA ACA        1344
      Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                  435                 440                 445

      GAT AAA TGG ATT GGA GGG TCC CCC CCA GCT GAC CAG ACC CTG GTC ATC        1392
 30   Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile
                  450                 455                 460

      AAG ACA TTC CGC TTC CTG TCA CAG AAA CTC TTT ATC TCC GTC TCA GTT        1440
      Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile Ser Val Ser Val
 35   465                 470                 475                 480

      CTC TCC AGC CTG GGC ATT GTC CTA GCT GTT GTC TGT CTG TCC TTT AAC        1488
      Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn
                  485                 490                 495
 40
      ATC TAC AAC TCA CAT GTC CGT TAT ATC CAG AAC TCA CAG CCC AAC CTG        1536
      Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu
                  500                 505                 510
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SUBSTITUTE SHEET (RULE 26)

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AAC AAC CTG ACT GCT GTG GGC TGC TCA CTG GCT TTA GCT GCT GTC TTC      1584
Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu Ala Ala Val Phe
        515                     520                 525

CCC CTG GGG CTC GAT GGT TAC CAC ATT GGG AGG AAC CAG TTT CCT TTC      1632
Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Asn Gln Phe Pro Phe
        530                 535                 540

GTC TGC CAG GCC CGC CTC TGG CTC CTG GGC CTG GGC TTT AGT CTG GGC      1680
Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly
545                 550                 555                 560

TAC GGT TCC ATG TTC ACC AAG ATT TGG TGG GTC CAC ACG GTC TTC ACA      1728
Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His Thr Val Phe Thr
                565                 570                 575

AAG AAG GAA GAA AAG AAG GAG TGG AGG AAG ACT CTG GAA CCC TGG AAG      1776
Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys
                580                 585                 590

CTG TAT GCC ACA GTG GGC CTG CTG GTG GGC ATG GAT GTC CTC ACT CTC      1824
Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp Val Leu Thr Leu
        595                 600                 605

GCC ATC TGG CAG ATC GTG GAC CCT CTG CAC CGG ACC ATT GAG ACA TTT      1872
Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr Ile Glu Thr Phe
        610                 615                 620

GCC AAG GAG GAA CCT AAG GAA GAT ATT GAC GTC TCT ATT CTG CCC CAG      1920
Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser Ile Leu Pro Gln
625                 630                 635                 640

CTG GAG CAT TGC AGC TCC AGG AAG ATG AAT ACA TGG CTT GGC ATT TTC      1968
Leu Glu His Cys Ser Ser Arg Lys Met Asn Thr Trp Leu Gly Ile Phe
                645                 650                 655

TAT GGT TAC AAG GGG CTG CTG CTG CTG CTG GGA ATC TTC CTT GCT TAT      2016
Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr
                660                 665                 670

GAG ACC AAG AGT GTG TCC ACT GAG AAG ATC AAT GAT CAC CGG GCT GTG      2064
Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp His Arg Ala Val
```

675   680   685

```
GGC ATG GCT ATC TAC AAT GTG GCA GTC CTG TGC CTC ATC ACT GCT CCT      2112
Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu Ile Thr Ala Pro
    690                     695                 700

GTC ACC ATG ATT CTG TCC AGC CAG CAG GAT GCA GCC TTT GCC TTT GCC      2160
Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala
705                     710                 715                 720

TCT CTT GCC ATA GTT TTC TCC TCC TAT ATC ACT CTT GTT GTG CTC TTT      2208
Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu Val Val Leu Phe
                    725                 730                 735

GTG CCC AAG ATG CGC AGG CTG ATC ACC CGA GGG GAA TGG CAG TCG GAG      2256
Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu
            740                 745                 750

GCG CAG GAC ACC ATG AAG ACA GGG TCA TCG ACC AAC AAC AAC GAG GAG      2304
Ala Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu
            755                 760                 765

GAG AAG TCC CGG CTG TTG GAG AAG GAG AAC CGT GAA CTG GAA AAG ATC      2352
Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile
    770                 775                 780

ATT GCT GAG AAA GAG GAG CGT GTC TCT GAA CTG CGC CAT CAA CTC CAG      2400
Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln
785                 790                 795                 800

TCT CGG CAG CAG CTC CGC TCC CGG CGC CAC CCA CCG ACA CCC CCA GAA      2448
Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu
                805                 810                 815

CCC TCT GGG GGC CTG CCC AGG GGA CCC CCT GAG CCC CCC GAC CGG CTT      2496
Pro Ser Gly Gly Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu
                820                 825                 830

AGC TGT GAT GGG AGT CGA GTG CAT TTG CTT TAT AAG TGA                  2535
Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys  *
                835                 840
```

(2) INFORMATION FOR SEQ ID NO: 51:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 844 amino acids
       (B) TYPE: amino acid
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:

```
Met Gly Pro Gly Ala Pro Phe Ala Arg Val Gly Trp Pro Leu Pro Leu
 1               5                  10                  15

Leu Val Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
             20                  25                  30

Pro His Leu Pro Arg Pro His Ser Arg Val Pro Pro His Pro Ser Ser
             35                  40                  45

Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
     50                  55                  60

Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
 65                  70                  75                  80

Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
                 85                  90                  95

Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
                100                 105                 110

Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
         115                 120                 125

Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
     130                 135                 140

Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
145                 150                 155                 160

Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
                 165                 170                 175
```

```
    Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
            180                 185                 190

 5  Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
            195                 200                 205

    Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
            210                 215                 220
10
    Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
    225                 230                 235                 240

    Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
15              245                 250                 255

    Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
                260                 265                 270

20  Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp
            275                 280                 285

    Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly
            290                 295                 300
25
    His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
    305                 310                 315                 320

    Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
30                  325                 330                 335

    Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
            340                 345                 350

35  Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
            355                 360                 365

    Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn
            370                 375                 380
40
    Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
    385                 390                 395                 400
```

Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
                    405   410   415

Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
                    420   425   430

Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                    435   440   445

Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile
        450   455   460

Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile Ser Val Ser Val
465   470   475   480

Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn
                    485   490   495

Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu
                    500   505   510

Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu Ala Ala Val Phe
            515   520   525

Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Asn Gln Phe Pro Phe
        530   535   540

Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly
545   550   555   560

Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His Thr Val Phe Thr
                565   570   575

Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys
                580   585   590

Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp Val Leu Thr Leu
        595   600   605

Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr Ile Glu Thr Phe
        610   615   620

Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser Ile Leu Pro Gln

625   630   635   640

Leu Glu His Cys Ser Ser Arg Lys Met Asn Thr Trp Leu Gly Ile Phe
                645   650   655

Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr
                660   665   670

Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp His Arg Ala Val
                675   680   685

Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu Ile Thr Ala Pro
            690   695   700

Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala
705   710   715   720

Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu Val Val Leu Phe
                725   730   735

Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu
                740   745   750

Ala Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu
            755   760   765

Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile
        770   775   780

Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln
785   790   795   800

Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu
                805   810   815

Pro Ser Gly Gly Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu
            820   825   830

Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys
            835   840

(2) INFORMATION FOR SEQ ID NO: 52:

SUBSTITUTE SHEET (RULE 26)

(i) SEQUENCE CHARACTERISTICS:
    (A) LENGTH: 2895 base pairs
    (B) TYPE: nucleic acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
    (A) ORGANISM: Canis familiaris

(ix) FEATURE:
    (A) NAME/KEY: CDS
    (B) LOCATION:1..2895

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:


```
ATG CTG CTG CTG CTC CTG CCG CTG GCG CTG GCG CCG CTC TTC CTC CGC        48
Met Leu Leu Leu Leu Leu Pro Leu Ala Leu Ala Pro Leu Phe Leu Arg
 1               5                   10                  15


CCC CCG GGC GCG GGC GGG GCA CAG ACC CCC AAC GCC ACC TCG GAA GGT        96
Pro Pro Gly Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly
             20                  25                  30


TGC CAG ATC ATA CAC CCG CCT TGG GAA GGG GGT ATC AGG TAC AGG GGC       144
Cys Gln Ile Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly
             35                  40                  45


CTG ACT CGT GAC CAG GTG AAG GCT ATC AAC TTC CTG CCG GTG GAC TAT       192
Leu Thr Arg Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr
         50                  55                  60


GAG ATT GAG TAT GTG TGC CGG GGA GAG CGA GAG GTG GTG GGG CCC AAG       240
Glu Ile Glu Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys
 65                  70                  75                  80


GTC CGA AAG TGC CTG GCC AAT GGC TCC TGG ACA GAT ATG GAC ACA CCC       288
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       Val Arg Lys Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro          —
                        85              90              95


     AGC CGC TGT GTC CGA ATC TGT TCC AAG TCA TAT TTG GCC CTG GAA AAT         336
   5 Ser Arg Cys Val Arg Ile Cys Ser Lys Ser Tyr Leu Ala Leu Glu Asn
                    100             105             110


     GGG AAG GTC TTC CTG ACG GGT GGG GAC CTC CCC GCT CTG GAT GGA GCC         384
     Gly Lys Val Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala
  10           115             120             125


     CGG GTG GAT TTC CGG TGT GAC CCT GAC TTC CAT CTT GTG GGC AGC TCC         432
     Arg Val Asp Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser
              130             135             140
  15
     CGG AGT ATC TGT AGT CAG GGC CAG TGG AGC ACT CCC AAG CCC CAC TGC         480
     Arg Ser Ile Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys
     145             150             155             160


  20 CAG GTG AGC CGA ACG CCG CAC TCA GAG CGG CGA GCG GTG TAC ATC GGG         528
     Gln Val Ser Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly
                    165             170             175


     GCG CTG TTT CCC ATG AGC GGG GGC TGG CCG GGG GGC CAG GCC TGC CAG         576
  25 Ala Leu Phe Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln
                    180             185             190


     CCC GCG GTG GAG ATG GCG CTG GAG GAC GTG AAT AGC CGC AGG GAC ATC         624
     Pro Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile
  30           195             200             205


     CTG CCG GAC TAC GAG CTC AAG CTC ATC CAC CAC GAC AGC AAG TGT GAC         672
     Leu Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp
              210             215             220
  35
     CCA GGC CAA GCT ACC AAG TAC CTG TAT GAA CTG CTC TAC AAC GAC CCC         720
     Pro Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro
     225             230             235             240


  40 ATC AAG ATC ATC CTC ATG CCT GGC TGC AGC TCT GTC TCC ACG CTT GTG         768
     Ile Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val
                    245             250             255
```

SUBSTITUTE SHEET (RULE 26)

```
    GCT GAG GCT GCC AGG ATG TGG AAC CTC ATT GTG CTC TCC TAT GGT TCC       816
    Ala Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser
                    260                 265                 270


5   AGC TCA CCA GCT CTG TCC AAC CGG CAG CGC TTT CCT ACC TTC TTC CGA       864
    Ser Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg
                    275                 280                 285


    ACT CAT CCC TCG GCC ACG CTC CAC AAC CCT ACG CGA GTG AAG CTC TTT       912
10  Thr His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe
                    290                 295                 300


    GAG AAG TGG GGC TGG AGG AAG ATT GCC ACC ATC CAG CAG ACC ACC GAG       960
    Glu Lys Trp Gly Trp Arg Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu
15  305                 310                 315                 320


    GTG TTC ACA TCG ACT CTG GAC GAC CTA GAG GAA CGA GTG AAG GAG GCT      1008
    Val Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala
                        325                 330                 335
20
    GGG ATT GAG ATT ACT TTC CGC CAG AGC TTC TTC TCA GAT CCT GCC GTG      1056
    Gly Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val
                        340                 345                 350


25  CCT GTC AAG AAC CTC AAG CGC CAG GAT GCC CGA ATC ATC GTG GGA CTT      1104
    Pro Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu
                    355                 360                 365


    TTC TAT GAG ACT GAA GCC CGG AAA GTG TTC TGT GAG GTA TAC AAG GAG      1152
30  Phe Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu
                    370                 375                 380


    CGG CTC TTT GGG AAG AAG TAT GTG TGG TTC CTC ATT GGG TGG TAT GCT      1200
    Arg Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala
35  385                 390                 395                 400


    GAC AAT TGG TTC AAG ACC TAC GAC CCC TCC ATC AAC TGC ACA GTG GAT      1248
    Asp Asn Trp Phe Lys Thr Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp
                    405                 410                 415
40
    GAG ATG ACC GAG GCT GTG GAA GGC CAC ATC ACC ACT GAG ATT GTC ATG      1296
    Glu Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met
                    420                 425                 430
```

SUBSTITUTE SHEET (RULE 26)

```
CTG AAC CCA GCC AAC ACC CGC AGC ATC TCC AAC ATG ACA TCC CAG GAG      1344
Leu Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu
        435                 440                 445

TTT GTG GAG AAA CTG ACC AAG AGA CTC AAG AGA CAC CCT GAG GAG ACA      1392
Phe Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr
        450                 455                 460

GGC GGC TTC CAG GAG GCA CCG CTG GCC TAT GAT GCC ATC TGG GCC TTG      1440
Gly Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu
465                 470                 475                 480

GCA TTG GCC CTG AAC AAG ACA TCT GGA GGG AGC GGC CGT TCG GGG GTG      1488
Ala Leu Ala Leu Asn Lys Thr Ser Gly Gly Ser Gly Arg Ser Gly Val
                485                 490                 495

CGC CTG GAA GAC TTC AAC TAC AAC AAC CAG ACG ATC ACA GAC CAA ATC      1536
Arg Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile
                500                 505                 510

TAC CGC GCA ATG AAC TCC TCG TCC TTT GAG GGT GTC TCT GGC CAC GTG      1584
Tyr Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val
        515                 520                 525

GTG TTT GAT GCC AGC GGC TCA CGG ATG GCC TGG ACT CTG ATT GAG CAG      1632
Val Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln
        530                 535                 540

CTG CAG GGT GGC AGC TAC AAG AAG ATC GGC TAC TAT GAC AGC ACC AAG      1680
Leu Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys
545                 550                 555                 560

GAT GAC CTT TCC TGG TCT AAA ACG GAC AAA TGG ATT GGA GGG GCC CCC      1728
Asp Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ala Pro
                565                 570                 575

CCG GCC GAC CAG ACC CTG GTC ATC AAG ACA TTT CGC TTC ATG TCA CAG      1776
Pro Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Met Ser Gln
                580                 585                 590

AAG CTC TTC ATT TCA GTC TCT GTC CTC TCC AGC CTG GGC ATT GTC CTG      1824
Lys Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu
```

```
                 595                    600                    605

     GCT GTG GTC TGT CTG TCC TTT AAC ATC TAC AAC TCT CAT GTC CGT TAC      1872
     Ala Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr
5        610                    615                    620


     ATC CAG AAC TCC CAG CCC AAC TTG AAC AAT CTG ACT GCT GTG GGC TGC      1920
     Ile Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys
     625                    630                    635                    640
10
     TCC CTG GCA TTG GCT GCC GTC TTC CCC CTG GGG CTA GAT GGG TAC CAC      1968
     Ser Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His
                        645                    650                    655


15   ATC GGG AGA AGC CAG TTT CCT TTT GTG TGT CAG GCA CGC CTC TGG CTC      2016
     Ile Gly Arg Ser Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu
                    660                    665                    670


     CTG GGT CTG GGC TTC AGT CTG GGC TAT GGC TCC ATG TTC ACG AAG ATC      2064
20   Leu Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile
                    675                    680                    685


     TGG TGG GTC CAC ACG GTC TTC ACT AAG AAG GAG GAG AAG AAG GAG TGG      2112
     Trp Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp
25       690                    695                    700


     AGG AAG ACC CTG GAG CCC TGG AAG CTG TAC ACC ACA GTG GGC TTG CTA      2160
     Arg Lys Thr Leu Glu Pro Trp Lys Leu Tyr Thr Thr Val Gly Leu Leu
     705                    710                    715                    720
30
     GTG GGC ATG GAT GTC CTC ACT CTT GCC ATT TGG CAG ATG GTA GAC CCC      2208
     Val Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Met Val Asp Pro
                        725                    730                    735


35   TTG CAC CGG ACC ATT GAG ACT TTT GCC AAG GAG GAA CCA AAG GAA GAT      2256
     Leu His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp
                        740                    745                    750


     ATT GAT GTG TCC ATC CTG CCC CAG CTG GAG CAC TGC AGC TCC AAG AAA      2304
40   Ile Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Lys Lys
                        755                    760                    765


     ATG AAC ACC TGG CTT GGC ATT TTC TAT GGT TAC AAG GGG CTG CTG CTG      2352
```

SUBSTITUTE SHEET (RULE 26)

```
    Met Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu
        770             775             780

    CTG CTA GGC ATC TTT CTT GCT TAT GAG ACC AAG AGC GTG TCT ACT GAG    2400
    Leu Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu
    785             790             795             800

    AAG ATC AAT GAC CAC CGG GCT GTG GGC ATG GCC ATG TAC AAC GTG GCG    2448
    Lys Ile Asn Asp His Arg Ala Val Gly Met Ala Met Tyr Asn Val Ala
                805             810             815

    GTC CTG TGC CTC ATC ACT GCC CCG GTC ACC ATG ATC CTG TCC AGC CAG    2496
    Val Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln
                820             825             830

    CAG GAT GCA GCT TTC GCC TTT GCA GCT CTT GCC ATA GTG TTC TCC TCC    2544
    Gln Asp Ala Ala Phe Ala Phe Ala Ala Leu Ala Ile Val Phe Ser Ser
                835             840             845

    TAC ATC ACT CTG GTC GTT CTG TTC GTG CCG AAG ATG CGC AGG TTG ATC    2592
    Tyr Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile
        850             855             860

    ACC CGG GGT GAG TGG CAG TCG GAG GCG CAG GAT ACC ATG AAA ACG GGG    2640
    Thr Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly
    865             870             875             880

    TCG TCG ACC AAC AAC AAT GAG GAA GAG AAG TCC CGA CTG TTG GAG AAG    2688
    Ser Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys
                885             890             895

    GAG AAC CGG GAG CTG GAG AAG ATC ATT GCT GAG AAA GAG GAG CGA GTG    2736
    Glu Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val
                900             905             910

    TCC GAG CTG CGC CAT CAG CTT CGT TCT CGG CAG CAG CTG CGC CCT CGG    2784
    Ser Glu Leu Arg His Gln Leu Arg Ser Arg Gln Gln Leu Arg Pro Arg
            915             920             925

    CGT CAC CCC CCG ACG CCC CCA GAC CCC TCA GGG GGC CTG CCC AGG GGA    2832
    Arg His Pro Pro Thr Pro Pro Asp Pro Ser Gly Gly Leu Pro Arg Gly
            930             935             940
```

```
CCC CAT GAG CCC CCT GAC CGG CTC AGC TGT GAC GGG AGC CGG GTT CAC        2880
Pro His Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His
945             950             955             960

TTG CTG TAC AAG TGA                                                    2895
Leu Leu Tyr Lys  *
                965
```

(2) INFORMATION FOR SEQ ID NO: 53:

      (i) SEQUENCE CHARACTERISTICS:
         (A) LENGTH: 964 amino acids
         (B) TYPE: amino acid
         (D) TOPOLOGY: linear

      (ii) MOLECULE TYPE: protein

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:

```
Met Leu Leu Leu Leu Leu Pro Leu Ala Leu Ala Pro Leu Phe Leu Arg
 1               5              10              15

Pro Pro Gly Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly
            20              25              30

Cys Gln Ile Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly
            35              40              45

Leu Thr Arg Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr
            50              55              60

Glu Ile Glu Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys
65              70              75              80

Val Arg Lys Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro
                85              90              95

Ser Arg Cys Val Arg Ile Cys Ser Lys Ser Tyr Leu Ala Leu Glu Asn
                100             105             110

Gly Lys Val Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala
            115             120             125
```

```
     Arg Val Asp Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser
         130             135             140

 5   Arg Ser Ile Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys
         145             150             155             160

     Gln Val Ser Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly
                 165             170             175
10
     Ala Leu Phe Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln
                 180             185             190

     Pro Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile
15               195             200             205

     Leu Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp
         210             215             220

20   Pro Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro
         225             230             235             240

     Ile Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val
                 245             250             255
25
     Ala Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser
                 260             265             270

     Ser Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg
30               275             280             285

     Thr His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe
         290             295             300

35   Glu Lys Trp Gly Trp Arg Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu
         305             310             315             320

     Val Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala
                 325             330             335
40
     Gly Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val
                 340             345             350
```

SUBSTITUTE SHEET (RULE 26)

```
     Pro Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu
         355                 360             365


     Phe Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu
  5      370             375             380


     Arg Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala
     385             390             395                 400


 10  Asp Asn Trp Phe Lys Thr Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp
                 405             410             415


     Glu Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met
                 420             425             430
 15
     Leu Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu
                 435             440             445


     Phe Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr
 20      450             455             460


     Gly Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu
     465             470             475                 480


 25  Ala Leu Ala Leu Asn Lys Thr Ser Gly Gly Ser Gly Arg Ser Gly Val
                 485             490             495


     Arg Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile
                 500             505             510
 30
     Tyr Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val
             515             520             525


     Val Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln
 35      530             535             540


     Leu Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys
     545             550             555                 560


 40  Asp Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ala Pro
                 565             570             575


     Pro Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Met Ser Gln
```

                    580   585   590

    Lys Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu
            595   600   605

    Ala Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr
            610   615   620

    Ile Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys
    625   630   635   640

    Ser Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His
                    645   650   655

    Ile Gly Arg Ser Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu
                    660   665   670

    Leu Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile
                    675   680   685

    Trp Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp
            690   695   700

    Arg Lys Thr Leu Glu Pro Trp Lys Leu Tyr Thr Thr Val Gly Leu Leu
    705   710   715   720

    Val Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Met Val Asp Pro
                    725   730   735

    Leu His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp
                    740   745   750

    Ile Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Lys Lys
                    755   760   765

    Met Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu
            770   775   780

    Leu Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu
    785   790   795   800

    Lys Ile Asn Asp His Arg Ala Val Gly Met Ala Met Tyr Asn Val Ala
                    805   810   815

_____

Val Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln
        820   825   830

5   Gln Asp Ala Ala Phe Ala Phe Ala Ala Leu Ala Ile Val Phe Ser Ser
            835   840   845

Tyr Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile
    850   855   860
10
Thr Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly
865   870   875   880

Ser Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys
15   885   890   895

Glu Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val
            900   905   910

20 Ser Glu Leu Arg His Gln Leu Arg Ser Arg Gln Gln Leu Arg Pro Arg
            915   920   925

Arg His Pro Pro Thr Pro Pro Asp Pro Ser Gly Gly Leu Pro Arg Gly
    930   935   940
25
Pro His Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His
945   950   955   960

Leu Leu Tyr Lys
30

(2) INFORMATION FOR SEQ ID NO: 54:

        (i) SEQUENCE CHARACTERISTICS:
35   (A) LENGTH: 1737 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

40   (ii) MOLECULE TYPE: cDNA to mRNA

        (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
    (A) ORGANISM: Homo sapiens

(ix) FEATURE:
    (A) NAME/KEY: CDS
    (B) LOCATION:1..1737

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:

```
ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC            48
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1           5                  10                  15

GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC            96
Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
            20                  25                  30

ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG           144
Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35                  40                  45

GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG           192
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
            50                  55                  60

TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG           240
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65                  70                  75                  80

TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT           288
Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
            85                  90                  95

GTC CGA ATC TGC TCC AAG TCT TAT TTG ACC CTG GAA AAT GGG AAG GTT           336
Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
            100                 105                 110

TTC CTG ACG GGT GGG GAC CTC CCA GCT CTG GAC GGA GCC CGG GTG GAT           384
Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
            115                 120                 125
```

```
    TTC CGG TGT GAC CCC GAC TTC CAT CTG GTG GGC AGC TCC CGG AGC ATC        432
    Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile
        130             135             140

5   TGT AGT CAG GGC CAG TGG AGC ACC CCC AAG CCC CAC TGC CAG GTG AAT        480
    Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn
    145             150             155             160

    CGA ACG CCA CAC TCA GAA CGG CGC GCA GTG TAC ATC GGG GCA CTG TTT        528
10  Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe
                165             170             175

    CCC ATG AGC GGG GGC TGG CCA GGG GGC CAG GCC TGC CAG CCC GCG GTG        576
    Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val
15              180             185             190

    GAG ATG GCG CTG GAG GAC GTG AAT AGC CGC AGG GAC ATC CTG CCG GAC        624
    Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp
                195             200             205
20
    TAT GAG CTC AAG CTC ATC CAC CAC GAC AGC AAG TGT GAT CCA GGC CAA        672
    Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln
        210             215             220

25  GCC ACC AAG TAC CTA TAT GAG CTG CTC TAC AAC GAC CCT ATC AAG ATC        720
    Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile
    225             230             235             240

    ATC CTT ATG CCT GGC TGC AGC TCT GTC TCC ACG CTG GTG GCT GAG GCT        768
30  Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala
                245             250             255

    GCT AGG ATG TGG AAC CTC ATT GTG CTT TCC TAT GGC TCC AGC TCA CCA        816
    Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro
35              260             265             270

    GCC CTG TCA AAC CGG CAG CGT TTC CCC ACT TTC TTC CGA ACG CAC CCA        864
    Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro
             275             280             285
40
    TCA GCC ACA CTC CAC AAC CCT ACC CGC GTG AAA CTC TTT GAA AAG TGG        912
    Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp
        290             295             300
```

```
GGC TGG AAG AAG ATT GCT ACC ATC CAG CAG ACC ACT GAG GTC TTC ACT          960
Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr
305                 310             315                 320

TCG ACT CTG GAC GAC CTG GAG GAA CGA GTG AAG GAG GCT GGA ATT GAG         1008
Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu
                325             330                 335

ATT ACT TTC CGC CAG AGT TTC TTC TCA GAT CCA GCT GTG CCC GTC AAA         1056
Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys
            340             345             350

AAC CTG AAG CGC CAG GAT GCC CGA ATC ATC GTG GGA CTT TTC TAT GAG         1104
Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu
            355             360             365

ACT GAA GCC CGG AAA GTT TTT TGT GAG GTG TAC AAG GAG CGT CTC TTT         1152
Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe
    370             375             380

GGG AAG AAG TAC GTC TGG TTC CTC ATT GGG TGG TAT GCT GAC AAT TGG         1200
Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp
385             390             395                 400

TTC AAG ATC TAC GAC CCT TCT ATC AAC TGC ACA GTG GAT GAG ATG ACT         1248
Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr
                405             410                 415

GAG GCG GTG GAG GGC CAC ATC ACA ACT GAG ATT GTC ATG CTG AAT CCT         1296
Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro
                420             425                 430

GCC AAT ACC CGC AGC ATT TCC AAC ATG ACA TCC CAG GAA TTT GTG GAG         1344
Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu
                435             440             445

AAA CTA ACC AAG CGA CTG AAA AGA CAC CCT GAG GAG ACA GGA GGC TTC         1392
Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe
    450             455             460

CAG GAG GCA CCG CTG GCC TAT GAT GCC ATC TGG GCC TTG GCA CTG GCC         1440
Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala
```

```
      465                470                475                480

      CTG AAC AAG ACA TCT GGA GGA GGC GGC CGT TCT GGT GTG CGC CTG GAG      1488
      Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu
 5                    485                490                495


      GAC TTC AAC TAC AAC AAC CAG ACC ATT ACC GAC CAA ATC TAC CGG GCA      1536
      Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala
                500                505                510
10
      ATG AAC TCT TCG TCC TTT GAG GGT GTC TCT GGC CAT GTG GTG TTT GAT      1584
      Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp
                515                520                525


15    GCC AGC GGC TCT CGG ATG GCA TGG ACG CTT ATC GAG CAG CTT CAG GGT      1632
      Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly
                530                535                540


      GGC AGC TAC AAG AAG ATT GGC TAC TAT GAC AGC ACC AAG GAT GAT CTT      1680
20    Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu
      545                550                555                560


      TCC TGG TCC AAA ACA GAT AAA TGG ATT GTT ATA TCC AGA ACT CAC AGC      1728
      Ser Trp Ser Lys Thr Asp Lys Trp Ile Val Ile Ser Arg Thr His Ser
25                   565                570                575


      CCA ACC TGA                                                          1737
      Pro Thr  *
```

30

(2) INFORMATION FOR SEQ ID NO: 55:

          (i) SEQUENCE CHARACTERISTICS:
35   (A) LENGTH: 578 amino acids
              (B) TYPE: amino acid
              (D) TOPOLOGY: linear

       (ii) MOLECULE TYPE: protein
40

       (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 55:

Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly

SUBSTITUTE SHEET (RULE 26)

```
          1              5                  10                 15

        Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                    20                  25                  30
  5
        Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
                    35                  40                  45

        Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
  10          50                  55                  60

        Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
              65                  70                  75                  80

  15    Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                        85                  90                  95

        Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
                    100                 105                 110
  20
        Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
                    115                 120                 125

        Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser Arg Ser Ile
  25          130                 135                 140

        Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys Gln Val Asn
        145                 150                 155                 160

  30    Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe
                        165                 170                 175

        Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val
                    180                 185                 190
  35
        Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp
                    195                 200                 205

        Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro Gly Gln
  40          210                 215                 220

        Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile
        225                 230                 235                 240
```

SUBSTITUTE SHEET (RULE 26)

```
    Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala
                    245             250             255

  5 Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro
                    260             265             270

    Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro
                    275             280             285
 10
    Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp
                    290             295             300

    Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr
 15 305             310             315             320

    Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu
                    325             330             335

 20 Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys
                    340             345             350

    Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu
                    355             360             365
 25
    Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe
                    370             375             380

    Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp
 30 385             390             395             400

    Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr
                    405             410             415

 35 Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro
                    420             425             430

    Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu
                    435             440             445
 40
    Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe
                    450             455             460
```

SUBSTITUTE SHEET (RULE 26)

Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala
465   470   475   480

Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu
                485   490   495

Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala
            500   505   510

Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp
        515   520   525

Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly
    530   535   540

Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu
545   550   555   560

Ser Trp Ser Lys Thr Asp Lys Trp Ile Val Ile Ser Arg Thr His Ser
            565   570   575

Pro Thr

(2) INFORMATION FOR SEQ ID NO: 56:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 1386 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: cDNA to mRNA

        (iii) HYPOTHETICAL: NO

        (iv) ANTI-SENSE: NO

        (vi) ORIGINAL SOURCE:
            (A) ORGANISM: Homo sapiens

        (ix) FEATURE:

H1865-1 WO SEQ   75

(A) NAME/KEY: CDS
(B) LOCATION:1..1386

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 56:

```
ATG GGG CCC GGG GCC CCT TTT GCC CGG GTG GGG TGG CCA CTG CCG CTT      48
Met Gly Pro Gly Ala Pro Phe Ala Arg Val Gly Trp Pro Leu Pro Leu
 1               5                  10                  15

CTG GTT GTG ATG GCG GCA GGG GTG GCT CCG GTG TGG GCC TCC CAC TCC      96
Leu Val Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
            20                  25                  30

CCC CAT CTC CCG CGG CCT CAC TCG CGG GTC CCC CCG CAC CCC TCC TCA     144
Pro His Leu Pro Arg Pro His Ser Arg Val Pro Pro His Pro Ser Ser
        35                  40                  45

GAA CGG CGC GCA GTG TAC ATC GGG GCA CTG TTT CCC ATG AGC GGG GGC     192
Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
    50                  55                  60

TGG CCA GGG GGC CAG GCC TGC CAG CCC GCG GTG GAG ATG GCG CTG GAG     240
Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
65                  70                  75                  80

GAC GTG AAT AGC CGC AGG GAC ATC CTG CCG GAC TAT GAG CTC AAG CTC     288
Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
                85                  90                  95

ATC CAC CAC GAC AGC AAG TGT GAT CCA GGC CAA GCC ACC AAG TAC CTA     336
Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
            100                 105                 110

TAT GAG CTG CTC TAC AAC GAC CCT ATC AAG ATC ATC CTT ATG CCT GGC     384
Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
        115                 120                 125

TGC AGC TCT GTC TCC ACG CTG GTG GCT GAG GCT GCT AGG ATG TGG AAC     432
Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
        130                 135                 140

CTC ATT GTG CTT TCC TAT GGC TCC AGC TCA CCA GCC CTG TCA AAC CGG     480
Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
```

145   150   155   160

```
CAG CGT TTC CCC ACT TTC TTC CGA ACG CAC CCA TCA GCC ACA CTC CAC          528
Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
            165                    170                    175
```

```
AAC CCT ACC CGC GTG AAA CTC TTT GAA AAG TGG GGC TGG AAG AAG ATT          576
Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
            180                    185                    190
```

```
GCT ACC ATC CAG CAG ACC ACT GAG GTC TTC ACT TCG ACT CTG GAC GAC          624
Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
            195                    200                    205
```

```
CTG GAG GAA CGA GTG AAG GAG GCT GGA ATT GAG ATT ACT TTC CGC CAG          672
Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
        210                    215                    220
```

```
AGT TTC TTC TCA GAT CCA GCT GTG CCC GTC AAA AAC CTG AAG CGC CAG          720
Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
225                    230                    235                    240
```

```
GAT GCC CGA ATC ATC GTG GGA CTT TTC TAT GAG ACT GAA GCC CGG AAA          768
Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
            245                    250                    255
```

```
GTT TTT TGT GAG GTG TAC AAG GAG CGT CTC TTT GGG AAG AAG TAC GTC          816
Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
            260                    265                    270
```

```
TGG TTC CTC ATT GGG TGG TAT GCT GAC AAT TGG TTC AAG ATC TAC GAC          864
Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp
            275                    280                    285
```

```
CCT TCT ATC AAC TGC ACA GTG GAT GAG ATG ACT GAG GCG GTG GAG GGC          912
Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly
            290                    295                    300
```

```
CAC ATC ACA ACT GAG ATT GTC ATG CTG AAT CCT GCC AAT ACC CGC AGC          960
His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
305                    310                    315                    320
```

```
ATT TCC AAC ATG ACA TCC CAG GAA TTT GTG GAG AAA CTA ACC AAG CGA         1008
```

Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
                325   330   335

CTG AAA AGA CAC CCT GAG GAG ACA GGA GGC TTC CAG GAG GCA CCG CTG   1056
Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
                340   345   350

GCC TAT GAT GCC ATC TGG GCC TTG GCA CTG GCC CTG AAC AAG ACA TCT   1104
Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
                355   360   365

GGA GGA GGC GGC CGT TCT GGT GTG CGC CTG GAG GAC TTC AAC TAC AAC   1152
Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn
                370   375   380

AAC CAG ACC ATT ACC GAC CAA ATC TAC CGG GCA ATG AAC TCT TCG TCC   1200
Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
385   390   395   400

TTT GAG GGT GTC TCT GGC CAT GTG GTG TTT GAT GCC AGC GGC TCT CGG   1248
Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
                405   410   415

ATG GCA TGG ACG CTT ATC GAG CAG CTT CAG GGT GGC AGC TAC AAG AAG   1296
Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
                420   425   430

ATT GGC TAC TAT GAC AGC ACC AAG GAT GAT CTT TCC TGG TCC AAA ACA   1344
Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                435   440   445

GAT AAA TGG ATT GTT ATA TCC AGA ACT CAC AGC CCA ACC TGA   1386
Asp Lys Trp Ile Val Ile Ser Arg Thr His Ser Pro Thr *
450   455   460

(2) INFORMATION FOR SEQ ID NO: 57:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 461 amino acids
        (B) TYPE: amino acid
        (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 57:

```
Met Gly Pro Gly Ala Pro Phe Ala Arg Val Gly Trp Pro Leu Pro Leu
 1               5                  10                  15


Leu Val Val Met Ala Ala Gly Val Ala Pro Val Trp Ala Ser His Ser
            20                  25                  30


Pro His Leu Pro Arg Pro His Ser Arg Val Pro Pro His Pro Ser Ser
            35                  40                  45


Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
        50                  55                  60


Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
65                  70                  75                  80


Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
                85                  90                  95


Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
            100                 105                 110


Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
        115                 120                 125


Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
        130                 135                 140


Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
145                 150                 155                 160


Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
            165                 170                 175


Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
            180                 185                 190


Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
            195                 200                 205


Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
```

                210   215   220

        Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
        225   230   235   240

        Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
                        245   250   255

        Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
                    260   265   270

        Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp
                    275   280   285

        Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly
                290   295   300

        His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
        305   310   315   320

        Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
                        325   330   335

        Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
                        340   345   350

        Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
                    355   360   365

        Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn
                370   375   380

        Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
        385   390   395   400

        Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
                        405   410   415

        Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
                    420   425   430

        Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                    435   440   445

```
Asp Lys Trp Ile Val Ile Ser Arg Thr His Ser Pro Thr
    450             455         460
```

(2) INFORMATION FOR SEQ ID NO: 58:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 1746 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA to mRNA

    (iii) HYPOTHETICAL: NO

    (iv) ANTI-SENSE: NO

    (vi) ORIGINAL SOURCE:
        (A) ORGANISM: Canis familiaris

    (ix) FEATURE:
        (A) NAME/KEY: CDS
        (B) LOCATION:1..1746

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 58:

```
ATG CTG CTG CTG CTC CTG CCG CTG GCG CTG GCG CCG CTC TTC CTC CGC      48
Met Leu Leu Leu Leu Leu Pro Leu Ala Leu Ala Pro Leu Phe Leu Arg
 1           5             10              15

CCC CCG GGC GCG GGC GGG GCA CAG ACC CCC AAC GCC ACC TCG GAA GGT      96
Pro Pro Gly Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly
            20              25              30

TGC CAG ATC ATA CAC CCG CCT TGG GAA GGG GGT ATC AGG TAC AGG GGC     144
Cys Gln Ile Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly
            35              40              45

CTG ACT CGT GAC CAG GTG AAG GCT ATC AAC TTC CTG CCG GTG GAC TAT     192
Leu Thr Arg Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr
            50              55              60
```

```
    GAG ATT GAG TAT GTG TGC CGG GGA GAG CGA GAG GTG GTG GGG CCC AAG      240
    Glu Ile Glu Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys
    65              70              75              80
5
    GTC CGA AAG TGC CTG GCC AAT GGC TCC TGG ACA GAT ATG GAC ACA CCC      288
    Val Arg Lys Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro
                85              90              95

10  AGC CGC TGT GTC CGA ATC TGT TCC AAG TCA TAT TTG GCC CTG GAA AAT      336
    Ser Arg Cys Val Arg Ile Cys Ser Lys Ser Tyr Leu Ala Leu Glu Asn
                100             105             110

    GGG AAG GTC TTC CTG ACG GGT GGG GAC CTC CCC GCT CTG GAT GGA GCC      384
15  Gly Lys Val Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala
                115             120             125

    CGG GTG GAT TTC CGG TGT GAC CCT GAC TTC CAT CTT GTG GGC AGC TCC      432
    Arg Val Asp Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser
20  130             135             140

    CGG AGT ATC TGT AGT CAG GGC CAG TGG AGC ACT CCC AAG CCC CAC TGC      480
    Arg Ser Ile Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys
    145             150             155             160
25
    CAG GTG AGC CGA ACG CCG CAC TCA GAG CGG CGA GCG GTG TAC ATC GGG      528
    Gln Val Ser Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly
                165             170             175

30  GCG CTG TTT CCC ATG AGC GGG GGC TGG CCG GGG GGC CAG GCC TGC CAG      576
    Ala Leu Phe Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln
                180             185             190

    CCC GCG GTG GAG ATG GCG CTG GAG GAC GTG AAT AGC CGC AGG GAC ATC      624
35  Pro Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile
                195             200             205

    CTG CCG GAC TAC GAG CTC AAG CTC ATC CAC CAC GAC AGC AAG TGT GAC      672
    Leu Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp
40  210             215             220

    CCA GGC CAA GCT ACC AAG TAC CTG TAT GAA CTG CTC TAC AAC GAC CCC      720
    Pro Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro
```

225   230   235   240

ATC AAG ATC ATC CTC ATG CCT GGC TGC AGC TCT GTC TCC ACG CTT GTG   768
Ile Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val
5   245   250   255

GCT GAG GCT GCC AGG ATG TGG AAC CTC ATT GTG CTC TCC TAT GGT TCC   816
Ala Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser
               260   265   270
10

AGC TCA CCA GCT CTG TCC AAC CGG CAG CGC TTT CCT ACC TTC TTC CGA   864
Ser Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg
               275   280   285

15 ACT CAT CCC TCG GCC ACG CTC CAC AAC CCT ACG CGA GTG AAG CTC TTT   912
Thr His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe
               290   295   300

GAG AAG TGG GGC TGG AGG AAG ATT GCC ACC ATC CAG CAG ACC ACC GAG   960
20 Glu Lys Trp Gly Trp Arg Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu
305   310   315   320

GTG TTC ACA TCG ACT CTG GAC GAC CTA GAG GAA CGA GTG AAG GAG GCT   1008
Val Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala
25   325   330   335

GGG ATT GAG ATT ACT TTC CGC CAG AGC TTC TTC TCA GAT CCT GCC GTG   1056
Gly Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val
               340   345   350
30

CCT GTC AAG AAC CTC AAG CGC CAG GAT GCC CGA ATC ATC GTG GGA CTT   1104
Pro Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu
               355   360   365

35 TTC TAT GAG ACT GAA GCC CGG AAA GTG TTC TGT GAG GTA TAC AAG GAG   1152
Phe Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu
               370   375   380

CGG CTC TTT GGG AAG AAG TAT GTG TGG TTC CTC ATT GGG TGG TAT GCT   1200
40 Arg Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala
385   390   395   400

GAC AAT TGG TTC AAG ACC TAC GAC CCC TCC ATC AAC TGC ACA GTG GAT   1248

```
           Asp Asn Trp Phe Lys Thr Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp
                       405             410             415

     5     GAG ATG ACC GAG GCT GTG GAA GGC CAC ATC ACC ACT GAG ATT GTC ATG    1296
           Glu Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met
                       420             425             430

           CTG AAC CCA GCC AAC ACC CGC AGC ATC TCC AAC ATG ACA TCC CAG GAG    1344
           Leu Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu
    10                 435             440             445

           TTT GTG GAG AAA CTG ACC AAG AGA CTC AAG AGA CAC CCT GAG GAG ACA    1392
           Phe Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr
                       450             455             460

    15
           GGC GGC TTC CAG GAG GCA CCG CTG GCC TAT GAT GCC ATC TGG GCC TTG    1440
           Gly Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu
           465             470             475             480

    20     GCA TTG GCC CTG AAC AAG ACA TCT GGA GGG AGC GGC CGT TCG GGG GTG    1488
           Ala Leu Ala Leu Asn Lys Thr Ser Gly Gly Ser Gly Arg Ser Gly Val
                       485             490             495

           CGC CTG GAA GAC TTC AAC TAC AAC AAC CAG ACG ATC ACA GAC CAA ATC    1536
    25     Arg Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile
                       500             505             510

           TAC CGC GCA ATG AAC TCC TCG TCC TTT GAG GGT GTC TCT GGC CAC GTG    1584
           Tyr Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val
    30                 515             520             525

           GTG TTT GAT GCC AGC GGC TCA CGG ATG GCC TGG ACT CTG ATT GAG CAG    1632
           Val Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln
                       530             535             540

    35
           CTG CAG GGT GGC AGC TAC AAG AAG ATC GGC TAC TAT GAC AGC ACC AAG    1680
           Leu Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys
           545             550             555             560

    40     GAT GAC CTT TCC TGG TCT AAA ACG GAC AAA TGG ATT GTT ACA TCC AGA    1728
           Asp Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Val Thr Ser Arg
                       565             570             575
```

SUBSTITUTE SHEET (RULE 26)

ACT CCC AGC CCA ACT TGA   1746
Thr Pro Ser Pro Thr *
                580

(2) INFORMATION FOR SEQ ID NO: 59:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 581 amino acids
            (B) TYPE: amino acid
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 59:

Met Leu Leu Leu Leu Leu Pro Leu Ala Leu Ala Pro Leu Phe Leu Arg
 1   5   10   15

Pro Pro Gly Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly
                20   25   30

Cys Gln Ile Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly
            35   40   45

Leu Thr Arg Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr
        50   55   60

Glu Ile Glu Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys
 65   70   75   80

Val Arg Lys Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro
                85   90   95

Ser Arg Cys Val Arg Ile Cys Ser Lys Ser Tyr Leu Ala Leu Glu Asn
            100   105   110

Gly Lys Val Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala
            115   120   125

Arg Val Asp Phe Arg Cys Asp Pro Asp Phe His Leu Val Gly Ser Ser
        130   135   140

Arg Ser Ile Cys Ser Gln Gly Gln Trp Ser Thr Pro Lys Pro His Cys
145   150   155   160

5   Gln Val Ser Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly
                 165   170   175

     Ala Leu Phe Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln
                 180   185   190
10
     Pro Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile
                 195   200   205

     Leu Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp
15   210   215   220

     Pro Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro
     225   230   235   240

20   Ile Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val
                 245   250   255

     Ala Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser
                 260   265   270
25
     Ser Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg
             275   280   285

     Thr His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe
30   290   295   300

     Glu Lys Trp Gly Trp Arg Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu
     305   310   315   320

35   Val Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala
                 325   330   335

     Gly Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val
                 340   345   350
40
     Pro Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu
                 355   360   365

SUBSTITUTE SHEET (RULE 26)

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        Phe Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu
            370             375             380

        Arg Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala
 5      385             390             395             400

        Asp Asn Trp Phe Lys Thr Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp
                        405             410             415

        Glu Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met
 10             420             425             430

        Leu Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu
                435             440             445

 15
        Phe Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr
            450             455             460

        Gly Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu
 20     465             470             475             480

        Ala Leu Ala Leu Asn Lys Thr Ser Gly Gly Ser Gly Arg Ser Gly Val
                485             490             495

 25     Arg Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile
                500             505             510

        Tyr Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val
                515             520             525
 30
        Val Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln
            530             535             540

        Leu Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys
 35     545             550             555             560

        Asp Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Val Thr Ser Arg
                        565             570             575

 40     Thr Pro Ser Pro Thr
                580
```

SUBSTITUTE SHEET (RULE 26)

((2) INFORMATION FOR SEQ ID NO: 60:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 16862 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: double
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA (genomic)

    (iii) HYPOTHETICAL: NO

    (iv) ANTI-SENSE: NO

    (vi) ORIGINAL SOURCE:
        (A) ORGANISM: Homo sapiens

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:3415..3440

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:3441..3903

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:3904..3988

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:3989..4689

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:4690..4893

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:4894..5645

    (ix) FEATURE:
        (A) NAME/KEY: exon

(B) LOCATION:5646..5831

(ix) FEATURE:
    (A) NAME/KEY: intron
    (B) LOCATION:5832..7181

(ix) FEATURE:
    (A) NAME/KEY: exon
    (B) LOCATION:7182..7202

(ix) FEATURE:
    (A) NAME/KEY: intron
    (B) LOCATION:7203..8307

(ix) FEATURE:
    (A) NAME/KEY: exon
    (B) LOCATION:8308..8803

(ix) FEATURE:
    (A) NAME/KEY: intron
    (B) LOCATION:8804..12266

(ix) FEATURE:
    (A) NAME/KEY: exon
    (B) LOCATION:12267..12401

(ix) FEATURE:
    (A) NAME/KEY: intron
    (B) LOCATION:12402..12815

(ix) FEATURE:
    (A) NAME/KEY: exon
    (B) LOCATION:12816..12986

(ix) FEATURE:
    (A) NAME/KEY: intron
    (B) LOCATION:12987..14085

(ix) FEATURE:
    (A) NAME/KEY: exon
    (B) LOCATION:14086..14187

(ix) FEATURE:

        (A) NAME/KEY: intron
        (B) LOCATION:14188..14473

     (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:14474..14539

     (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:14540..14998

     (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:14999..15190

     (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:15191..16862

     (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 60:

GATCATATTA ATTTGAAGGT GGCGGGGCAG GATGGTTCTG TGGTGCAGTT TAAGATTAAG   60

AGGCATACAC CACTTAGTAA ACTAATGAAA GCCTATTGTG AACGACAGGG ATTGTCAATG   120

AGGCAGATCA GATTCCGATT CGACGGGCAA CCAATGAAAC AGACACACCT GCACAGTTGG   180

AAATGGAGGA TGAAGATACA ATTGATGTGT TCCAACAGCA GACGGGAGGT GTCTACTGAA   240

AAGGGAACCT GCTTCTTTAC TCCAGAACTC TGTTCTTTAA AGACCAAGAT TACATTCTCA   300

ATTAGAAAAC TGCAATTTGC TTCCACCACA TCCTGACTAC TACCGTATAG TTTTCTCTAT   360

TCTTTCATTT CCCCCTTCCC CATTCCTTTA CTGTACATAA AGTAACTGGT ATATGTGCAC   420

AAGCATATTA CTTTTTTTTT TTAAAACTAA ACAGCCAATG GTATGTTTTG ATTGACATCA   480

AGTGGAGACG GGGGGGAAAA TACTGATTCT GTGAAAATAC CCCCTTTCTC CATTAGTGGC   540

ATGCTCATTC AGCTCTTATC TTTATATTCC AGTAAGTTAT TTTGCTCTCA CTGTTTTAAC   600

AACAACAACA AAAAAACAAC AACATAAAAA TCCTTGCATA CCTTGTTCAA TTGGAGAATT   660

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TTAATGTTTT  TCATTTATCA  TTGTAAAACC  AAGGACAATT  TTATAACTTT  TTTGTACTTA    720

GCTGTTACAT  GCAGAGCAAT  CTGTCTTTAA  GTAGGGATAA  ATTACTCTAA  AACAAAAAAG    780

AATCCTAGAT  AGTTTTCCCT  TCAAGTCAAG  CGTCTTGTTG  TTTAAATAAA  CTTCTTGTTT    840

AAAAAAAAAA  AAAGTAAAAA  AGAAAAGTTA  TGCAACAATT  AATGGCCCAG  AGGCAATCCT    900

TGTTAACATT  TTGATGCATC  TTTTAGCTGT  TTTTTTTTTT  TTTTTTTTTT  TTGACTGAGT    960

TTGACTCTTG  TCACCCAGGC  TGAAGTGCAA  TGGCATGGCA  TGATCTTGGC  TCACTGCAAC   1020

CTCCGCCTCC  CGGGTTCAAG  TGATTCTCCT  GCCTCAGCCT  CCTGAGTAGC  TAGGATTACG   1080

GGCATGCACC  ACCATGCCTG  GCTAATTTTG  TATTTTTAGT  AGAGTTGGGG  CTTCTCCACA   1140

CTGGTCAGGC  TGGTCTCGAA  CTCCCAACCT  CAGGTGATAA  GGGAAGGGGC  ACTATTGACA   1200

TTTATGGTTG  GGGCAGAGGT  GTAAGATATT  CTTCAAAGCA  CTACCTACAT  GTTGAAGAAT   1260

TGTTCCTCAC  CCAGATTCTC  AAAAGTCCCC  CAGGACATTC  ACGTAGTGAA  AACCTGTGTT   1320

TAATTATCTG  AGCCTATAAC  TTAATACAGT  TTTAAAATTT  TTTTTAAAT   ATACAGTGAA   1380

CTTTCTAGGA  ATGCAATTAT  AGTTGTGTGT  AAAATTAGGG  AAAATTAACT  TTGCTACCAA   1440

GAGTTGTTCA  ACATTTTGTT  AAATCACTTC  ATTGATGGCA  ACATGCTGGA  GGTAGTTGAG   1500

TCACCAACTC  AGCACCTGGA  TCAGCCTGTG  TTGGTAGCAG  TTTCATCCCC  GTGGTTCTGT   1560

GAATAGGTGG  AAGCATCTGC  TTACTCCATC  AGGACTTCTA  GGGTAGTCGG  GCCTTGGCAC   1620

TCACACATTA  AAATACTGTT  TATGTTATTT  TATTGCAAGT  TACTTTCTT   TCATTTCCCC   1680

TTTACGTTAC  AGAAAGGGAA  GCATTTTGCT  TTCTGTTTAA  AGTTGTGTAT  GTAGGTAGGT   1740

TATATCATCT  AWGACTTTCT  CTCCCTCCTT  CCCTTTCTTT  TTGTTTGAGA  TGGAGTCTTG   1800

CTCTGTCACC  CAGGCTGGAG  TGCAGTGGTG  CGATCTTGGC  TCACTGCAAC  CTCTGCCTCC   1860

CGGGTTCAAG  CGATTCTGGT  GTCTCAGCTG  GGATTACAGG  CGCACACCAT  CACACCACGC   1920
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SUBSTITUTE SHEET (RULE 26)

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TAATTTTTCT ATTTTTAGTA GAGATGGGGT TTCGCCATGC TGGCCAGGCC AGGCTGGTCT    1980

CAAACTCCTG AGCTCAAGTG ATCAGTCCGC CTCGGCCTCC CAAAGTTCTG GGATTTCAGG    2040

CGTGAGCCTC ATCTATGAAT CTCAATTTAG GACAGTAAAA GTGTCATTAC AAAAATATTT    2100

ATTGTAAAAA AGGGTTGGAG GTTGAGAATC TCAATTCTAG TCAGTCTCTC AGTGTTTGGT    2160

TTCTTCCTAC CATTTTTCCC CCTAGGACCA GCCAGAAAGC AGCTTTTTTT TTGTCCCCCC    2220

CAACAAGGAG CCCACTGTTT CCTCTCCCAG CCCAAACTCA GGCCTACGAA CAACAACAGC    2280

ACTACACACA CACACACACA CACACACACA CACACACACA CACCCCTCCA CTTCAAGGTA    2340

TAGCCAAGAG CTTCTGGAGC CGTCAAAAAG GTCTGTACCT GCTGTCTTTA GAGCTTCCAG    2400

TTTGCCCTTG GTCAAGAAAT ACTGTTTGCT AGGCTCTGCT GGAGTACATC AGGTAATACT    2460

GGCTTCTAAA CCACCCTGAG GTTCTTTTCT CTTGTCCTTT TACTCCCTTC GTACTTCAAT    2520

TTCTCTCCTT GATGTCCCCC TCCCTGTTTT GTTTTTTGCC TCCAATCCGT TCTGCGCGTT    2580

CCCTGCAGAG CAGGCGAGTA GCAATGCTGC TGGACCATGG AGCTGCTCTA GTCTCCCAGA    2640

AATCTCTTCT ACACCCAACC CTTCTTGCGC TTAGGTGGTC CTCAGTCCCC CTCCCCCACC    2700

TCCTTCTGAC CCAGGCTTCT TTCTCGCCCT CCGGTCGCAG TTCTCCTGGG CATCTGCCTC    2760

TGCCTCTCTC CTCTCACCCG GATCTAGGGC TGCCTTCTCT TTGTGCAGCC GTCTTTCTCC    2820

ACCTTCATCC CAGACTCCCT GTCTCAGCGC CAGCTCCTCT GCCTTTGGCT CGGGTTCCCT    2880

CTCCCCCACC CCAGCTTCCA GTTGTTTGGC CCGCAGGTCC CTCGGCAGTG ACCGGCGCCC    2940

CCCGACGAGT GCGTGTGCAC CAGGGCACCT CCCTCTCCCC CACCTCTCAG CCCCGCGCCT    3000

CTCCACCGCC CGCCCCACCG CGCTGTGGGC GGTCCAGGGC GGGGCTGGGA TCCGGGGCGG    3060

CTCCCGGGGC TCGGGTTGTG GGAGGCGCCC TCTCCCCGGT CTTCCCCTCT CTTCCCCCCG    3120

CCCTGCCTTC CCTTGCACCC TCCTTCTTCC CTCCGCCCGG GAGCTCTCCC TGGTCCCCGG    3180

CGCCGCCTCC TTCCCTCCCG GCTCCCCGCT CCCCGCTCCC GTGGCTGCCG CCGCCCCGGG    3240
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SUBSTITUTE SHEET (RULE 26)

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GAAGAAGAGA CAGGGGTGGG GTTTGGGGGA AGCGAGAGAG GAGGGGAGAG ACCCTGGCCA    3300

GGCTGGAGCC TGGATTCGAG GGGAGGAGGG ACGGGAGGAG GAGAAAGGTG GAGGAGAAGG    3360

GAGGGGGGAG CGGGGAGGAG CGGCCGGGCC TGGGGCCTTG AGGCCCGGGG AGAGCCGGGG    3420

AGCCGGGCCC GCGCGCCGAG GTAAGAGCCA GGGCCCCGGG TTAGCAGGGC TCGGAGAGGG    3480

GGCGCGCGGC GTGGTGGGGG AGGGGGCAGT GGGCGCAGGG CCCAGCTGGG GGAAGCGGGG    3540

CTGGGGGAGA GGAGGAACCG CGGGGATGGA ATCGGGGAGC GCTGAGGCGG CCGATGCCGG    3600

GAGCGTGGGT AAGCCAGGCT TCTGCGAGCC GCGGGGGCCG GGGGAGAGGA GGTGGTGAGA    3660

GGTGGAGTCC GGGAGGGTTG GGGGCCGAGG GAGGCAGGAG GAGGGTGGGG ACAGGCTTTC    3720

TCTCCTCCTC TCCCCCCACC CCGCGCGGGG CTCCGCCCCC GCCTCCTCCG CGGGGCGCTC    3780

TCTTGGTCCC CAGGCTGAGC CCGGTCGGAG CCTGCGAGGC AACCGGCAAG AGGTCGAGTA    3840

GTCTCCGGGT GCGGGCCGCG CCGGCGGGGC TCGGTCCAGT CCTCATGGCC GCCTCTCACT    3900

TAGATGTTGC TGCTGCTGCT ACTGGCGCCA CTCTTCCTCC GCCCCCCGGG CGCGGGCGGG    3960

GCGCAGACCC CCAACGCCAC CTCAGAAGGT GCATCCTTCT TCGACGACCT CCGGCCCTCC    4020

TTCGCTCCAC TTCCCTTTCC CTGCATCTCC TCATTTCTGG TCCTCATCAC TATCCCATCA    4080

GTCCCACATA TCATCCCGGT CTGGCAACCC CTTCTGCTCG GCCCGACTTT ACTACTGCTG    4140

ACCTCCTTCT GTCACCCCAC GTTACTATCC AGCACCTCTT TTCTCTGCCC ACATTGCTAC    4200

ACTATACCAC CTTCCTGTGC ATTTTCTCCG CCTCAATCCC CTTTCCCAGC CCCACATTAC    4260

TACCTCAATT ACTCCCTTTT CTTGGTCCCA CTTTGCTGTC CAGATGATCT TATTAGCCTC    4320

CCTTTATCCT CCTATCCTAA TTCAACTGGA ATATCCTCAT TTAGCCTTTT TTTTTAAAGA    4380

AAAGCTCCAC CCACATATCA TACCCTTCAT GATTTCTTAA TTACTTTTCT TTCTTACCTC    4440 ᴜ

CACCCAGCAC CCTTCCCTCC CCACTTGTGG GTTCTCTCAT CAGCTTTAAC CCTGGCCCTT    4500
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SUBSTITUTE SHEET (RULE 26)

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TACTCTCTGT CCTTTAGCCA GGGGATCTGT ACCTGTCCCC ACTCCCACCC TCTAGTGCCC    4560

CATCCCTCTT CCTCTGTCCC CAGCCTGCCC ACAGACCACG CCCTACTCTC CCCTTCCTCC    4620

CACTGGGGAG CCTGCCTTTT CCTCTTTCCC ACCATTCCTC TCTGTATGCC TCCCCGACTC    4680

ACCCCTTAGG TTGCCAGATC ATACACCCGC CCTGGGAAGG GGGCATCAGG TACCGGGGCC    4740

TGACTCGGGA CCAGGTGAAG GCTATCAACT TCCTGCCAGT GGACTATGAG ATTGAGTATG    4800

TGTGCCGGGG GGAGCGCGAG GTGGTGGGGC CCAAGGTCCG CAAGTGCCTG GCCAACGGCT    4860

CCTGGACAGA TATGGACACA CCCAGCCGCT GTGGTGAGTA GCCTCGGAAG CCCCTCCCCT    4920

CTTCAAGACT ATTCCTTTTC CTGCCGCAAA CTTAGCATTA CTGCTTGCAA GTCAGCACTT    4980

TAAATCCAGT ATACCAAAAT TCACAAATAC ATTTATTGAA TGACTACTAC ATAAGAGCAA    5040

TTTTGCTCTG TGCGGTTGGA GGTAGTAGAG CTAGCAGCCT GCACAGTTCA TTTCATCCTC    5100

CCTTCATTAG GCCACTGATC ATTGGCCTAT AACATTGATA ATTCATCTTG TCAGTTATTC    5160

TCTTTGAGGA TCATTAGTGG CAGATGATGA CAAAAAAATT CTAAAATGAT TTCATCACAT    5220

TTTTGAATAC CTCTGTCACC AACCCAGAGA CCATATGCCC AAGAAACAAA AGCCAGTTTA    5280

ATATTAATAG AAGCCAACTA TAATAAGAAA AGCAAATCTG ATTGTGCATC CAAAGTTATA    5340

TACATCTACA TATTTCAAAG CCAGAGAACC GCCCACTGTA GCTGACTTTG AAGAGATCCC    5400

ATTTTGTGTG CTTATAGCCC CATCTTGGGT TCCTAAAATG GTAATTTTTT TTTTCTTTTG    5460

GGAATGTGTG GATGCTTGCA CAGGTAAGGG AGGATTGGAA GATAGGTAGG CAAATCCTTT    5520

TCACATGTGA TTTTCTTTAG AGCAGGATGC TTGTGGACCC AAACCTGCAC CTGAGTCCCC    5580

TGCTCTTTAA AGGGAAAGAG CCTTCTTCAA CTCGCCTCTC TTCTTATTTT CCTATCTCTC    5640

CACAGTCCGA ATCTGCTCCA AGTCTTATTT GACCCTGGAA AATGGGAAGG TTTTCCTGAC    5700

GGGTGGGGAC CTCCCAGCTC TGGACGGAGC CCGGGTGGAT TTCCGGTGTG ACCCCGACTT    5760

CCATCTGGTG GGCAGCTCCC GGAGCATCTG TAGTCAGGGC CAGTGGAGCA CCCCCAAGCC    5820
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SUBSTITUTE SHEET (RULE 26)

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CCACTGCCAG GGTGAGGGGA ACAGCTGCCT GCATGCAGCT GATGAGGACG CTTGTGTGAG   5880

GATGGGAGTG GGGTGGGAAT GGATAATGGG AAAGAATGGA GAGCTATAAA AATGTGGGGG   5940

AGGACACTGG AAAGGGGAGA TGAAAGTCCC TTTTTCCTCC ATCACCTGCC TCAAACTTCC   6000

TCTTGCAGTC CCCGGTATCC TCTGTAGGTT GGGGGCTTCC TTCCTTTACC TTTTAAAAAA   6060

ATCTTCCTGC TCCCGATTCT TAGACCTCAC GTTTTCTCTT TTCCTTTATG AATCTCACCT   6120

CTCTCACCTT CTTCAGGTTT AAATACTCCA ATTTTCCCTT TCTCTAAACT TAGAAATTTC   6180

CATGCATCAC CCTCTTCTAG AATTCATCCC TCACCATTCC TTATATAATT GATTTATTGT   6240

AAAGACTCAG AAATAAATCA AACATTCTAC TAAGAAAAAT TGAGAAGGGG AGCTCTGGGG   6300

GTGGAAACAT ATTAGGGTAA AAGACTTAAA ATTGGAGGCA GCATTATCAG AAGATGAAGA   6360

ACAACTCAGG GATGGGGTGG GAAGAAGACA GGTCCTTTTC TGKACTTCCT AGACAACCTC   6420

CATTATTCCC TAAGGGAATC AGTGTTGTGT CTGTCTACYT TTTTTTTTTT TTTTTTGCCA   6480

CGTAATTTTA CAAACTCTCC CTTTTCTAGG CACCCGAACT CTCTGCCATC TTCTCTCCTG   6540

GGATGCAGTC ATCCCATTTG TATGCCTCAT ACTTCCTCTA CCCTGGTAGA TTCTTTCAAG   6600

ATCCTTGGGC TTTACTTTCC TCACATAACT CAGTTATTCT GCTTCTAGTT TACCATTTTA   6660

TTCTGGAAAT TGAGAGTCCC ATCCAGGGGT GGACTTATGA CACTACTGAA ACTTAGACTT   6720

CAAGGTTCCT CACCTACAGG GCCCTCTTCC TGTGCTCTAA TAATATAGAG GGCTCGATGG   6780

ATATGTGTTC ATATGGTAAC AGGCTTTTGT AAAAATTGCA GAAATAAGAT TTTAACAGCA   6840

ATTGCTTAAA GCCAATTGTA TGTGTAATTT TTTTTCTTAA AGACTCCCAA TTTTGTAATA   6900

TTCAGGCACC ACAGAACCAA GATCTGCCCC AAACTTAGCT ATTGGCATTC CCGTCTCAAA   6960

TTCTGTTGTC CTATGAAAAA TCGAAGAAGA AAATAAGTCC TGACCCCCTT ACCCCCAGAC   7020

CCACCTTGTT CTTATCCCCA GGCACCCTCC CCTCAGAAAC GCAGGCTTCT GCTCTCCCCG   7080
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SUBSTITUTE SHEET (RULE 26)

GTCTTCAGCA TGGACAGGTG TGGGAGGGGG CTGGGGATCA GGCCAGGGAA GCTGGGCGCC   7140

AGTGGTAACT CTTCTCTGAT CCCCGTCTTT CCTGCTGCCA GTGAATCGAA CGCCACACTC   7200

5   AGGTGAGATG AGAAACCCTT ACCGCGCGCA CTGCAATGCC CTCCCCTTCA CTCTGCACCC   7260

TCCACCCCCC TGAAATTCTG CCCTTAGGCT ACGGGGCGTC GTCCTTTCGC ACCTTCCCCA   7320

ACCCACCCCA GTTTGCGGCC ACCCCCTTCC CTCCCTACCT GTTTCCTGCC TCCAGTCCCG   7380

10   GTTTTCCACG AGGCTGCGGT CTCTCCTTGT CCCTGCTTGG CTACACTTCC CTGGGCTCCA   7440

CCTCCTCCCA GACTGAGCCT CGCCGGTGTC AGGCAGAGCC CAGCAGARGG CGGCAGGGTG   7500

15   CTGGGAGACC CTGAGCTCCC ACCACGTTTT CCCCTGTGGG GTTCCTTGCG ACCTTCGCTG   7560

GAACCTTTTC CAGCCTGCTG CCTCCTAGGA TTTCACCTAA TGGACTTTCT CAGCCTGTCC   7620

CACCCATCCC AACCCTGGCC AGGCCTCTCG CGCTCTTCCC CACATCTTTT CCTTCCGTGT   7680

20   ACCCCTTCCC TCGTCTTTTC TCAATTCCAT GTCCTGTCTC CCTTTCTTAG GCTTCTGTCT   7740

ACCCAGCCCC AGGCTCCCTT CCACGACCCC ACCACTCCCT CAAACCAGCC TCCCTTCCGT   7800

25   ACCCAACTCG TTCCCTCCAA AACCGTTTCC TCTCCCCCAC ATCCTCAGTG CTTCACTGTA   7860

TCGACTCATA CTCCCACTTC AGACCTCAGG CGCCAGCCCC GTTTCTCTCC CGTCCCACTC   7920

GCATCCTTCC CTTCCTACCC TGGTTCCTCC GTGCTTCAGC CTCCCGCGGC TCCCTCCGCC   7980

30   CACCCCGCCC TCCTGGCACG CCCCGTCCCC ATTTCTCCTC CCCTCGGGTC CCCTTAAGTG   8040

AGATCCCTCC CTTCCTCTTT CGTTCCTTTC CTCCTCGAGG TTGCATCCCC CCTCCCCTCC   8100

35   CCGCCCCTCC GACTGTCGCT CCCACCTCGG CGCTCGCTTC CCTCCCCGCC CCCTTCCTGC   8160

CTCCCCAGCT CCCGCCCGCC CCCCCACCCC CCGCTGCCGC GCGCCGCCCG TGACGTCAGA   8220

GCCCCCTCCC AGCCCCACAT CTCCCTCCTG CTCCTCCTCC TCCCCTCCGT CGGTCAGTCA   8280

40   GTCCGCGAGG AGAGTCCGCG GTGGCGGCGA CGGTGGCGAG AGCCGCGGGG GCCGTAGGAA   8340

GCCAACCTTC CCTGCTTCTC CGGGGCCCTC GCCCCCTCCT CCCCACAAAA TCAGGGATGG   8400

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AGGCGCCTCC  CCGGCACCCT  CTTAGCAGCC  CTCCCCGGGA  AAAGTGTCCC  CCCTGAGCTC    8460

CTAACGCTCC  CCAACAGCTA  CCCCTGCCCC  CCACGCCATG  GGGCCCGGGG  CCCCTTTTGC    8520

CCGGGTGGGG  TGGCCACTGC  CGCTTCTGGT  TGTGATGGCG  GCAGGGGTGG  CTCCGGTGTG    8580

GGCCTCCCAC  TCCCCCCATC  TCCCGCGGCC  TCACTCGCGG  GTCCCCCCGC  ACCCTCCTC     8640

AGAACGGCGC  GCAGTGTACA  TCGGGGCACT  GTTTCCCATG  AGCGGGGGCT  GGCCAGGGGG    8700

CCAGGCCTGC  CAGCCCGCGG  TGGAGATGGC  GCTGGAGGAC  GTGAATAGCC  GCAGGGACAT    8760

CCTGCCGGAC  TATGAGCTCA  AGCTCATCCA  CCACGACAGC  AAGGTAGCCC  TGGACATGGG    8820

GGTGGGTGGG  AGGTGGGGGC  TTGCGGGSCA  GGGGGCCAAG  CAAGCCTGCA  CGCGCCCCCA    8880

TCTGTCTGAG  TCGTCTCTGG  GATTGCGAGG  CAGACCCCTC  CCTTGTGTGA  CTGGCAGGAG    8940

ATGGGCTGGG  GGTGCAGGAG  CTTGGGAAGA  GTCGCAGGGG  CTGGAGGTCC  AAGATGAGGG    9000

TCTAGGGGCT  CAAGATGGTT  AAGCATGCTG  CAAGGCAGAC  CCTTCTGCCC  CGCTGCGGGA    9060

GTCTCGCAGA  AGTGTCGGGG  TTTGGAGAAA  CTGGTGGTGG  ATTTAAGGTA  TTAGGAGACA    9120

CTGATCCTCT  GAGGGAGTAA  ACTAACCCTG  GAATGGGTTG  GGGGTGGAGG  GAATGTCAGA    9180

GGTGGGGAGC  TGGATTGGGG  GGTTACATTT  ACCATGGTAA  CAAGGTAAAA  TCTTGGCGTA    9240

GGTTGGAGCT  GGAAGGAATA  GGGACAGAAT  GAGGAAAATT  TTGAGAGACT  TGAGAGCTCT    9300

AGTTTATTTA  TCTTAACAAA  ACAGCAAGGT  AGTGGTGAGC  CCTACCTGAC  TCCTTCTCAT    9360

CCTTCTATTC  CCAACCCTGT  TGAGCATTCC  CAGACTGTGG  GATAGATGGC  ATATGGTGAT    9420

TGGGGAAGGC  TAATGATCAA  GAGGTGGGCA  GAGGCACTGG  GAAAATGAAT  TGGATTGGGG    9480

ATCCACATGG  GAACCCCCAC  AATAGCATGG  GGATGAAGAA  GAGTCAACAT  ACAAGGAGAA    9540

GAGAACAGAA  AAGAATGGCA  GTGGGGGAGA  GGGGCAAGGA  GGTAGCGTGG  GGATAATGAG    9600

AGATCTTGGG  GCACCTTATG  GAACTTGGGT  CCTGACCTTC  CCTTCCCTTA  TAGCATTGTG    9660
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GCCTCTAGGA TGTGAGAAGG GAAATGGGAT GTAGGGATTA GGGAGGTGAG TTGAGGGAGA    9720

GAGAGAAGGT AAGCAAATTT GGGTCCAGGG GTATTAGGGG ATAGCTTATA ATGAGGTTTT    9780

TTTTCCCACC CCTCTCCCCT ACATGAATAA TTGGGGGTGC AGGGAAGGAT GTGACACAGG    9840

GAAGGAGATT TAAGATCTCA AATTTATCTT CACTGACATG TGGCCCCAGA GACTTAAGGA    9900

ATTGGGTTAG GGTGAAATAG AGTACACAAG GTGAGAATTT GGTGATCTTA CCAAATATCA    9960

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TTACTAATAG ACATCCTATC TTGGTGGATT CCTGAGCTGT AAGCTAACCC CAGAATGCCT   10320

ATGGGAAGAG CAGCAGGGTA CAGGAAAATA ATTAGGTATT AGGGTACGGG AGGCAGGAAG   10380

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AAAGATTTAC AAAGTTGCCC TAGTGGGAGG CATAAAGAGA AAACCTTCCA ATGTTGTTGA    11100

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TGCCAGAAAG GAGAAGAAAA CGGTAATTAA TGATGAAAGT GAGTAATTGA GAAAGGAACT    12180ᵤ

AATTTGTTCG AGAAAGATAA GAGCAGGAAT TGCAGACAGG GGAGGGGCCC CAGGAGAGCT    12240
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SUBSTITUTE SHEET (RULE 26)

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TGCCCTCATC TCCTCTTGTC TTTCAGTGTG ATCCAGGCCA AGCCACCAAG TACCTATATG    12300

AGCTGCTCTA CAACGACCCT ATCAAGATCA TCCTTATGCC TGGCTGCAGC TCTGTCTCCA    12360

CGCTGGTGGC TGAGGCTGCT AGGATGTGGA ACCTCATTGT GGTAAGCAGG GCTATGGGGG    12420

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ATGAGGGAGA GGAGAGAGAG GGGCAGAAAG GCAGCTGCAT GGATCTGGTA GTTGGTACTA    13500

AGAGAGAGAA GCCGACAGAC AAGGAGAGGT TGAGGGGGAA GAGGGAGATT TGGGGAGGTA    13560
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SUBSTITUTE SHEET (RULE 26)

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    TCTTTGGGTC TTCTATCCAC TGTGTTCAGT GGCCCTTTAA TCCTCCCCCA CTTTCACTCT   13680

5   GATTCAGACC ATTCTTCTCT GATCCTTTGT CTGTCTGCCC ATTTGCCTCT TGAGGTTGAC   13740

    ATCATGCTGT CTGTCCCAGT CCTTGCCTTG TCTTTTCCTG GTTCCTTTAT GTTTCTTTAC   13800

10  CCCATCTTTG CCTTCAGTGG TAGGAGTGGG TGAATGGAGT GGCTTCCCCC ACACAGAGCC   13860

    TCAGCAGGGG CTCACCATTC ACCTTCCCAC TTGGAATCCA CATCCTAAGA CCAGATGCCT   13920

    TCCCGAACTC CTCACTTCAG GGACAGAAGC TGTTGAAGGA AGGTTCAGAA TGGCTGCTTC   13980

15  TTTGCTCTAT CTGAGTATTG CTCTGAAATC CCCAGTTAAC CTCTCTGGTC TTTATTCCCT   14040

    CATGCACCCC GTGTTTTTCC AACTTGTTTT TTATTCCCAC CCAAGACTCT GGACGACCTG   14100

20  GAGGAACGAG TGAAGGAGGC TGGAATTGAG ATTACTTTCC GCCAGAGTTT CTTCTCAGAT   14160

    CCAGCTGTGC CCGTCAAAAA CCTGAAGGTC AGATGGCTGG GAGTGGTGGG CTCTGTTTAC   14220

    GGAGGGACCA AGCTGGGGGA CAGTGACTGG TTGGAGAGGA AAGCCAGGCG GGGGCAGGTT   14280

25  TTGATTCTCT GAGGCAATAG CATCTCCTGG GGAAGTTTAG CTCCATCTTC CAGTTGACGT   14340

    TTATTCACTA TACGTTGAGC GTTACCCTGC ACTAAGCACT TTGGGATGGG AAATCAAAGC   14400

30  TGTGAAGACA TCTGGCTTAG CCCCTCAGGC ATTCCCGGGC ATCCCTCAGG AGCTGTTTCT   14460

    TTCTCTGTTG TAGCGCCAGG ATGCCCGAAT CATCGTGGGA CTTTTCTATG AGACTGAAGC   14520

    CCGGAAAGTT TTTTGTGAGG TGGAGTTGGA TCTGAAGAGG GAGGGGCACT GGGTGGGAGT   14580

35  TTCCCTTGGT TTTCTTGTGG GGCCTCCTCT TGGCATCTGT GCCTGAGTTG ATAGCATATG   14640

    ATCTGAGGTG ACGATTCATA GGATGTCTCT GTCTGTTGGC TCTGACTGCA TCCCTTGTCT   14700

40  GCACACACAT GATACTTTCT TCAGATCTCA TTTTTCTACT GCTTTGTGTT TCCTGAGAAG   14760

    CCCATGAATT CCATCTGTCC TGACTGGCTG GAAAAGGCCA CTCAGAAATA CAGGGGCTGG   14820
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SUBSTITUTE SHEET (RULE 26)

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GTACAAGGAG CGTCTCTTTG GGAAGAAGTA CGTCTGGTTC CTCATTGGGT GGTATGCTGA    15060

CAATTGGTTC AAGATCTACG ACCCTTCTAT CAACTGCACA GTGGATGAGA TGACTGAGGC    15120

GGTGGAGGGC CACATCACAA CTGAGATTGT CATGCTGAAT CCTGCCAATA CCCGCAGCAT    15180

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ACTTATCTAC ATTTTGTAGA CCAGGAAAAT GAGACTCAGA GTGGTTTAAT GACTTGTCTC    16140
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ACTGCTCTGC TCATCACTTC CCATGGAAAA CCATGAAGCC TGACTAAAAA GTTTGTACTT   16260

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GAAGTTGACT CTGGTGGTGT GTTGTGATGA AAGATCTGCT GCCACATGGA CTCTGATGAT   16380

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AGAAAACAGG GATTTGGCTG GATCTAGTGG CTCACACCTG TAGTCCCCAG CACCTTGGGA   16680

GGCCAAGGCA GAGGATCACT GGAGCCCAGG AGTTCAAGAC CAGCCTGGGC AATATAGTGA   16740

GACCCCCAGC TCTAAACAAA AAGAGAGAGA GAGAGAACAG AGAGATGGTT AGGGACATAG   16800

AGGGACACCT GAGCATTGGG GTGGGAAGAC TTGGAAGGTC CCTTTCTGAC TTTGTGTCTA   16860

GA   16862

(2) INFORMATION FOR SEQ ID NO: 61:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 16707 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: double
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA (genomic)

    (iii) HYPOTHETICAL: NO

    (iv) ANTI-SENSE: NO.

    (vi) ORIGINAL SOURCE:
        (A) ORGANISM: Homo sapiens

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:1..2742

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:2743..2985

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:2986..3613

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:3614..3677

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:3678..5226

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:5227..5304

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:5305..6848

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:6849..6999

    (ix) FEATURE:
        (A) NAME/KEY: intron
        (B) LOCATION:7000..7494

    (ix) FEATURE:
        (A) NAME/KEY: exon
        (B) LOCATION:7495..7627

(B) LOCATION:11370..11591

(ix) FEATURE:
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    (B) LOCATION:11592..11735

(ix) FEATURE:
    (A) NAME/KEY: intron
    (B) LOCATION:11736..12512

(ix) FEATURE:
    (A) NAME/KEY: exon
    (B) LOCATION:12513..13999

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 61:

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AGCTAATTTT GGAATTTTTT TTTTTGAGAC AGAGTTTCAT TCTTATTGCC CAGGCTTGAG       60

TGCAATGGCG CGATCTTGGC TCACAGCAAC CTCCGCCTCC CAGGTTCAAG CCATTCTCCT      120

GCCTCAGCCT CCGGAGTAGC TGGGATTACA GGCATGCGCC ACCACACCCG GCTAATTTTG      180

TATTTTTAGT AGAGACAGGG TTTCTCCATG TTGCTCAGGC TGGTCTCGAA CTCCGGACCT      240

CAGGTGATCC ACCCGCCTCA GCCTCCCAAA GTGCTGGGAT TACAGGCGTG AGCCACCGTG      300

CCCAGCTAAT TTTTGTATTT TTCATAGAGA CAGGGTTTCA CCATGTTGGC CAGGCTGGTC      360

TTGAACTCCT GACCTCATGA TCTGCCCGCC TTGACCTCCC AAAGTCCTGA GATTACAGAT      420

GTGAGCCTCC GTGCCCAGGC CAAGTCTGGC TAATTTTTAA AAAAATTTTG TAGAGTTGGG      480

TCCTCTCTGT TTTGCCCAGT CTTGTCTCAA ACTCCTGGGC TCAAGGAATC CTCCTGCGTT      540

GGCCTCTGAA AATGAAAATG TTGGGATTAC AGGCGTGAGC CCCCTGTGCC TGGCTGCCTT      600

TTTTTTTTTT TTTTTTTAAA GGCAGAGTCT CACTCCATCG CCCAGGCTGA AGTGCAGTGG      660

CGTGATCTCT GCTCACTGCA ACCTCTGCCT CTTGAGTTCA AGCGATTCTT CTACCTCAGC      720

TTCCCAAGTA GCTGGGATTA CGGGAGCCCA CCAACACACC CAGCTAATTT TTGTATTTTT      780
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AGTAGAGACG GGTTTCACCA GGTTGGCCAG GCTGTCTGGA ATTCCTGACC TCAGGTGATC    840

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ACTTGTTTTT TATAATGCCT TTTTTTTTTT TTTTTGAGAC GGAGTCTTGC TCTGTCGCCC    960

AGGCTGGAGT GTAGTGGCGT CATCTCAGCT CACTGTAACC TCCACCTCCT GGGTTGAAGT   1020

GATTTTCTCA CCTCAGCCCT CAGCCTCCTG AGTAGTTGGG ACTGCAAGTG CACACCACCA   1080

TGCCCAGCTA ATTTTTTGTA TTTTAGTAGA GATGGGGTTT CACCATGTTG CCCAGCTGGT   1140

CTTTAACTCC TGAGCTCAGG CAGTCTGCTT ACCTTGGCCT CCCAAAGTGC TAGGATTAAA   1200

GGTGTGAGCC ACTGTGCCTG GCCTTTTTTT TTTTTTTTTT TTTTTGAGC AGTTTTAGTT   1260

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TGAGGTAAGG AAGGAATGAT GTGATTTTCT CCAGTATGTA GAATGCAGTT CCAAGAGGTT   1980

AAGTAATTTA CTTACAGTTA TTTAGCCAAA CAAGGTTACT GCAAGGTATA TGAAGTCAGG   2040

TCTCTTGACC CAGTTCATGA GAGAGTTAAA GGAACTATCA TTCTTTTTAG CTTTCATGGA   2100
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GCACACAAGA ATGGCAAGAA GTTAGCATGC TGAAGAAATA TCCTCCTGGC TGGCAAGCAG   2280

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ATTGGAATAT CCATGTCTCC TCCTTTACTC TGCTCTACCT TCCATCCTTT GCCACTAATT   2460

ATCCAGAGTG TTTGTCAAAA TTCTCTGTTT GCAGTTCTGA GCTAGCAACT GTACACACTA   2520

ACACCATCAG ACACAGCTAA TACCTACTCT AGTCTAGTAG CTTCCGATCT AAGGCAGACA   2580

CATGGGTATA GTTAAAGATT TTGAATGTAC ATGTGTCCAA TCTGACAACA GTAACACAAA   2640

CCATCCATTC AAGTAGAAGT GATTGAGTCA GAATTGGATT GCACCCCTTC CCCCACACCC   2700

ACACACATTT CAGTTCTTTC CTCATGATTT TTTCCTCCCA AGACATCCCA GGAATTTGTG   2760

GAGAAACTAA CCAAGCGACT GAAAAGACAC CCTGAGGAGA CAGGAGGCTT CCAGGAGGCA   2820

CCGCTGGCCT ATGATGCCAT CTGGGCCTTG GCACTGGCCC TGAACAAGAC ATCTGGAGGA   2880

GGCGGCCGTT CTGGTGTGCG CCTGGAGGAC TTCAACTACA ACAACCAGAC CATTACCGAC   2940

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GAGAACTATA GGATTTTGAA AGACAAAACA GTCTGAAAGG TCATCTTCTT ATTCCTTTTA   3300

AAATGAAAAG ATTAGTTTCC AGAGAGATTT GCTGACTTGC TTAGGCCACA CAACCAGAAG   3360
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SUBSTITUTE SHEET (RULE 26)

CCTGCTGGTG TTCTGTCTGG GGATTTTTTC CCATTCAAAT CTCATAAGTG AAGCTCCTTC   3420

TCCAAAGAAT AATGTTTCTA AAATCTAGGG TATGGGCATC TGGGGTATGT CCTATATGCA   3480

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CACCTCCCAA CTTCTGCCCT TCTCTTTTAA CTCTGTTCAT CAAGCTTGTA AATAATAATA   3840

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AACCTGTCTC TACCAAAAAT ACAAAAAAAA AAAAAAAAT TAGCTGGGTG TGGTGGCAGG   ·4080

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GGGAATCTGC CAAATTTCCT TGCTGTGTAA AGCTTCAATG TGTATAGCTT GGCTTTTGTA   4440

GATTGTATTT TCTTGAAACT TAGCACACAG GTATTTGCAG AACTTCTAGG AGTTAATTTT   4500

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GGTCCAAAAC AGATAAATGG ATTGGTGAGT GGATCTTGTT TGTATTTTCC TTCAGCCCCT   5340

CTCGACAGTC AAGGGAAAAA GTCATGCCTT TGAGTGAGGA TGGAATGGTA GAGACTGTTA   5400

GGTTGGAATG TGGCTGGCAG CTGGGCCAGG AGAAAGGGTT AAGTGAGAGT GAATACAACC   5460

CCTAAGGCGT GGGTAGGGGA GACTGGTGTA TTTGGAGAGG GAATAGGCGG TGGTTAGTAC   5520

TATTTTTAAT GGTGCATTGC TGGGGTAACT GGGGATTAGA GGCAGGGGGT GGGCAGAGGG   5580

CGGGAAATGG AAACTCCATT TGGGTTTCCC AGATGTCCTG GTGTCTTGAT ATATTTGAAC   5640

CAGCTACTTC AAGCCCAGAG CTGTCTCTTT GTCTGTCTCT GTCAGGAAAA CGGTTGCTTA   5700

AACTATGGAG GAGGAGGGAA AACCTCATGT AATTGTCATC TGCCAAAATG TGCTTTTTAT   5760

TTTTATATGT ATTTTTAAAA ATTTTCCTAT TTTTATGTAA TTTAGAGGTA GACGTGCAGT   5820

TGTGTTACAT GAATATATTG CATAGTGGTG AAGTCCGGGC GTTAGTGTG CCTGTCACCC   5880

GAACAGTGCA CCTTGTACCT AATAGGTAGT ATTACATCCC TCAAAATATA CTTTTTAAAG   5940

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AGAGAAAGCA AGCAGTTATT CTTTGTGTAC TTGGTCTAAA TGATAGGACA TAGGAGAGAA    6000

ACTGAAGGTG GACAAAAGGA AGGACCTACT GATAAAAGAA AGCCTCCTTG AGAATGAAGG    6060

GGAGGCTCAA CCATTGAAGA TGGCTGCCGT CTGCCCTGCC CAGCAGATAT CCAGTCATTC    6120

CCAGCACTGC TGGAGTTTTG CCCTTTTTTT TTTTTTTTTA CAATTCGAAT TTAGGACAAT    6180

GTTCTGGATT GCTATAAATG CTGCATGGCC TAAATTATTC TTTAAAAAAA AAACTAAGCA    6240

AATTGAAATT AGTTTTTTTT GGTGAACTCT GACAAATTTG AACTTCCCCC TAATAATAAC .  6300

TGGAAAACAT ATTTGGGAAT ATTACCCTGC CAGGATTAAA ATTTCAGATT AGCTTTCCTT    6360

CTTTTTTTGT TTGTCTTAAG AATAGGTGTC CACACTAGAT ACTTCAAGGC CTTTTTAGCT    6420

TTATGATTCC ATAATTGTCA TTTAAAACTT TGATTTGGGT TATAAGAAAC CTTATAACAT    6480

TTTTTAATGA TCCCCTTCTT TCTCCTCCCA TTTTCCTTTG CTGTAAGAAA GACAGAAAAA    6540

CTTAAAGAAC AAACAAAAAC AAAGACTACA ACTTTGGGGA CATGCCTCAG CATTTCCCAA    6600

CCTATGGATA GACCATTCAC TCCATCTTCT CATCTCATTT CTGGTTGCTT CCTAACGGCC    6660

CCAGTGGCAC TGAGCATTCT GCCTGCAGTA ACCTCTGTCC AGTGCAGTTA GGGCCTCATG    6720

TCCCCAGCCA ATGACTGAAT GTCCATCAGC AATCTAGTTC TTTGCCCTTT TCTCCTATCC    6780

CGTCTTCATT CCTTTGTCCT CCTTCCCTTC TCTTTTCCCT TCCCCTCTTC CTCCCCTGTG    6840

CCATGCAGGA GGGTCCCCCC CAGCTGACCA GACCCTGGTC ATCAAGACAT TCCGCTTCCT    6900

GTCACAGAAA CTCTTTATCT CCGTCTCAGT TCTCTCCAGC CTGGGCATTG TCCTAGCTGT    6960

TGTCTGTCTG TCCTTTAACA TCTACAACTC ACATGTCCGG TAAGTTTCTC TTCTGACGTT    7020

TTCCTTGTCT GCCTCTCTGA GATACTGATC ATGTTCCTGG ACAGGATGAG AATAAAACCT    7080

GTGTAACTCC CATGGCCATG TATCATGGAG TTTTTCATTC TGACTTGTTG AGAATGAAAA    7140

CAGGGAAACC AGATATAACC CCCACTCCTA CTCCAAAGTA GCTAACGGGA GGAAAAAAGA    7200

AAAGAAGAGA AAAAAACAAC CTTTGGGGCC AGGTCTCACA GTCTTGGACT CTACATAAAT    7260
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SUBSTITUTE SHEET (RULE 26)

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AGCCTGTATT CTAGTGGGGG CCTGTGCTTG GGAAGCCCTC TGCAACTCCA TCTTCAGCCC    7320

CATGACTGCA TTGCTCTGCC TCTCAAGGCT CCACTGTCTT CTCCAATCCT GTCTTCCTTT    7380

AGCCCCTGGC CCTGAAATTA GGGTCATGCC ATTGCGTGGT ATTTGGAGAG CTCAGCCTCC    7440

CTGGAGAAGA GGGGTAATTC TCTCTCCCTC TCACCCTCTC CACCTCTGCC CTAGTTATAT    7500

CCAGAACTCA CAGCCCAACC TGAACAACCT GACTGCTGTG GGCTGCTCAC TGGCTTTAGC    7560

TGCTGTCTTC CCCCTGGGGC TCGATGGTTA CCACATTGGG AGGAACCAGT TTCCTTTCGT    7620

CTGCCAGGTG AGGAGGTGGT GGGCAAATTC CTTACAGGAT GTGACTCTCC CACCCGTCTC    7680

AGGAGCACCT TCCATGATTT ATGATTCTCT GCCCTTCCTC CTCAGCTTTC CCTGACTCTT    7740

GTCCCTGTTC TTTCCTTCTA GCATCACCCC TCTGTTCTCT GTTTGGCTCT GTCCCTTCTT    7800

TCTGTGTCTG CAGGCCATTT TCATTCTGTA GTTTACTTGT CAGTTCCAAG GTTGCCATGG    7860

CAGSCCTYGC AGAGAAGAGG AGGGAGCCAT TGAAGGCAAA GGAAGGGGAT CTGCTCAAAG    7920

GTCTCCTGAA CAATGGTGGC TTGTCTGTGG TATGGGGGCT GAGAATCAGA ACTGTGGACT    7980

TTTTTTGGGA GCCTTTGTTG GGTTTGGAAG GATAGAAGCA GAGATGGAAA CACAGCAGAG    8040

AGTTGGGGGG AAGGGACCAC TGCCACACAG GGGAGGAGGG GCTCTGGGAC TGTTGGTACA    8100

TGGAAGGTTC TAGTGCTGTG GGGAGAGGCC AGCTTCAACA GTGATAGTTG AGTGGTTCTC    8160

TTTTCCACTG GTGGAAACAC CCACTCTTTC TCCTGATCTG CCTGCCTGTC CTTGCTCTCT    8220

CTTTTTCCTC TGCTCTGTGC TGTCCTGATC ATACATCTGT GCACATGGCA TTTCCATGCA    8280

CATGCACATG CAGTTCATCA GGAATCCTCT GTTCCCAGTG AGGCCAGAGT GCAGCTGGAG    8340

AAGCAGACAA TTAGCTGTAG TGCAATAGGA GAGGTTCCAG AGTAGGGATC TGCACAAAGT    8400

GCTTTGGGGG CAAAGAAGGG AACACAGTTC ACTGCTGGCG TGATTGGGTG GACCTCACTG    8460

AAGAGGTGGC ATTTGAATAC TGAAGGACAA ATAGGATTTT ATCAGCTAGA GAAATAGAGG    8520
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AAGGCTACTT CAGGGGCATA GGGAGCATCG TGTGGCTAGA AAATACATGA AAGAGAGTAG    8580

ATGAAGAGAA AGTGAGTAGT TCAGCATGGC TGGAGCGTGG GGTAGGTGTG GGGCTGGGAG    8640

ATGAGCCTAG CTGGACAGGT GGATGGGAGC ATGTTGTGAA GGGTCTGTGT CATATCCAGA    8700

AGTGTTCAGG CTATAACTTA TAGATATTGG GGAGTGGTTG GAGGTTTTTG GCCACTAAAG    8760

CCAGGAGGTT TTAGCAAGAT CACCCTGGTG GTGTGGAAGT AGAGGGTGGA TGGGAGGAAT    8820

TGTTCAAGGT GGGGAGACTG CTCTCCTCCT GCCGCTCCCC GTCCTGCTCA CATTTTCGCA    8880

TCCTCCCTGT GCCACCATGA GCTCCCTGCC CGTGCTCCCT GCCCACTCTC CCTTAGGGTT    8940

CTGCCCATCC TTACTGCAGT CCCGGCTACT ACTCTACCCT GTTCTGCCTG TGCCCTCTCT    9000

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GAGGAAGGTG AGCTGCTGCC CAATCCTCAG CCCCCARATC CTTGGCTCCT GGGGCACAGA    9180

GCATTTTCCC CTGACGTGCC TGTTCTCCCC ACATATTTAT CCAGACTCTG GAACCCTGGA    9240

AGCTGTATGC CACAGTGGGC CTGCTGGTGG GCATGGATGT CCTCACTCTC GCCATCTGGC    9300

AGATCGTGGA CCCTCTGCAC CGGACCATTG AGGTACCACT GGAGAGGAGG TGCTATGGTC    9360

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TGAAGCTACT TGGAGAGAGT GCCTTCCTCG TATTGGAAGC TCTTCCTTTC CTTCCTAGAA    9480

GGAGCCCCTC ATAGGCCTCC AGATTCAGCT GAAGAAAGGA AGGGGTGGGA ATCTGGGAAG    9540

GGTGTGTAGA ACTTCCAGGC ATCAGGGAAA GTGGGGAACA AGCACCTCCA AGGGTTCAGG    9600

AAAACATTCT TAGGCCTAGA ATGAGATTTG GCATCAGCAT TGAGGGTCTC ATAGGAAAAC    9660

AGTTGGAAGC CAGAGACTGA GAAGCGTTGA GGAGAGGAGG GGAGGCTGGC AACCATCTTT    9720

CTTGTGACCT TGTTTCTGCC CTAGACATTT GCCAAGGAGG AACCTAAGGA AGATATTGAC    9780

GTCTCTATTC TGCCCCAGCT GGAGCATTGC AGCTCCAGGA AGATGAATAC ATGGCTTGGT    9840
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SUBSTITUTE SHEET (RULE 26)

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GTGTGGGATG  TGGGCAAAGG  AGGGCAGGGA  TGCACAAAGG  CAGGAGGGAA  GGCAGGGGTA   9900

GAGGGCTTGG  AGGGAGAGGG  GTCTTTGGAA  GAGGAGGTAG  AGAGCTTGTC  AACCCAGTTT   9960

GAACACCCTA  CTCTTTGTTA  TTGCACTAAT  CTTTTCTGAG  AATAGGGGAG  AGTTGCTCTT  10020

TTGCTATGAG  GAGCTTAGGG  CCCAAAGCAC  AGAAAGCACA  GATGAAGAAC  TTGTGTTCAG  10080

CAGAGGAACA  AGTGGGGGTA  ACCCCACCTC  CAGACTTGAC  ATTATCTTTT  AGATCCCCCT  10140

TGGCCTTATT  AGCATTGTTC  GATTCATGGT  CACAAATTGC  AAACCTACCC  TCTGCCTGGA  10200

AAGCCACCTT  CCCACCTGTA  GGGTAAGGGT  GAGGCATGTG  TGGCCCAGAC  TGGCCTATTT  10260

CTAGATATTC  AACAAGCCCT  TGCCTGACTG  ACAGCAGCTT  GCCACCATTG  CTTTCCTGTG  10320

TGAATCCCAG  GAAAAAGTGA  TGTGGTCTGG  GCAAGTTGGG  TGGACATAAG  GGATAGGGGA  10380

CACAGGGTGA  GGTTTGCTAG  GTCAGAGGGG  TTGGATTGGA  GAGGAGGGCC  CCCTTTCCAT  10440

TTCAGAGTAG  GTGAAGGGCA  GAGAGGGGAT  GGGGATTGAG  TGAGGAGCAT  TGTGGTCCTT  10500

GTTGCTCAAG  TGACTCTCTC  CTGCCATCCT  AGGCATTTTC  TATGGTTAAC  AAGGGGCTGC  10560

TGCTGCTGCT  GGGAATCTTC  CTTGCTTATG  AGACCAAGAG  TGTGTCCACT  GAGAAGATCA  10620

ATGATCACCG  GGCTGTGGGC  ATGGCTATCT  ACAATGTGGC  AGTGAGCACT  GACCCCATGG  10680

CATTGACCCT  GTAGGCTGAC  CACAGCAGCC  CAGATATAGA  GGACTAGGAA  GAATCAATGC  10740

TAGATCTGGG  ATCGGTTGCT  TAGAAGTCTT  AAAAAGTTTG  TTAATTCTTC  AGGTCTATAA  10800

AGCACTTTAC  AGTTTACAAA  GCTCACTACA  GACATTGTAT  CATTAATCTT  GCAACTACCC  10860

AGTGAAGTAG  ATATTAGTAT  CCCCACTTTA  TAGGTGAGGA  AACAGAAACA  CAGAGACGTT  10920

AAATTGCTTG  TCTGTGGTTA  ATGGGCTGGA  CTCTATTGAC  ATTTCCTGCC  AGGGACCGAC  10980

TCTGGAGGAC  CCGGAATCTG  TGCATAGAGA  TCCTGGGAGT  TCCTGCCTTG  AGGGGAGGGG  11040

TTAACCAAGA  GTGAAAACTG  GTTTGGGACA  GTTTGAGATT  TTTCTCAATC  TATATTGAGG  11100
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SUBSTITUTE SHEET (RULE 26)

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ATGATCCTGA ATTTGGATCC TTTTCAAAGG GAAAGTTCAC CAGGAAACTG TCTGCATAGA    11160

CTCCCTCCCA TGGGAAGTAA ACTCTGGATC TTGTCTGAGC CTGCAGACCT GAGACTCCCT    11220

CAATGTGTCT TTCCCTCTAG GTCCTGTGCC TCATCACTGC TCCTGTCACC ATGATTCTGT    11280

CCAGCCAGCA GGATGCAGCC TTTGCCTTTG CCTCTCTTGC CATAGTTTTC TCCTCCTATA    11340

TCACTCTTGT TGTGCTCTTT GTGCCCAAGG TAAGGATCTG GCTTTTCTCC CACCCTCTTT    11400

GTTCCCATGT TCCCTCCATC CCTCCTTCCT ATATTACTGA GTTCCTCTGC CCTTCCGTTC    11460

ACCTCCTCT CACTCCTCCC CTTGTTTTGG GCCCAACTCT TATCAGCATT CCTTCCACCT     11520

CCAACCTTCC ATCAGCCAGT CACTAGTACA GTCCTTGCTG GGCCACCCCA CGCCCAAACA    11580

TTTGCCCCCA GATGCGCAGG CTGATCACCC GAGGGGAATG GCAGTCGGAG GCGCAGGACA    11640

CCATGAAGAC AGGGTCATCG ACCAACAACA ACGAGGAGGA GAAGTCCCGG CTGTTGGAGA    11700

AGGAGAACCG TGAACTGGAA AAGATCATTG CTGAGGTGCG GGGGTGGGTG TCAGGGTAGG    11760

GTGTTGGAGT GGTCCAGGAG GCTTGCGTCT TAGCTTGGGT TGTCTGAAGC CAAGCCTGAG    11820

ATACAGGGTC AGATGTTCTT GGCTCATGGA GGGAGGGTCC TAGGAGACAA CCTGTAAGGA    11880

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CCAGTGTTGG CCTGGCAGGT GGAAGGGCTC TGGAGTGGGA GCTATGTGGT TGACTCAGCC    12000

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GGGATGTTCC AACTGGGTTG ACACATCTCT CTGATTTATT GGAAGCTCTG TGCACTGACT    12240

TTTCTCTCCT TCCCCACTTT TTCCTTTTGT TTTTAAATTC TCTCTTATTT CCCTGATCGC    12300

ATTTTTTCTA TCGGTATCCT TATGTTCTCT GGCTTTTCTT GTTCTGTTTT GATTTCTCCT    12360

TTTAATTTAT TCTGTCCACT TACCCTACGT CCTCCCCCTA CATTTTTCTG TGCCCTTCCT    12420
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SUBSTITUTE SHEET (RULE 26)

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CTCTTTCCCT GTGCCCTTCC TCTCTTTCCC TCCTCCCCAC TCCTTCATCA CCTCCTCTTC   12480

TCCTACTATC CCAATTGTGC TTCTTCCTCC AGAAAGAGGA GCGTGTCTCT GAACTGCGCC   12540

ATCAACTCCA GTCTCGGCAG CAGCTCCGCT CCCGGCGCCA CCCACCGACA CCCCCAGAAC   12600

CCTCTGGGGG CCTGCCCAGG GGACCCCCTG AGCCCCCCGA CCGGCTTAGC TGTGATGGGA   12660

GTCGAGTGCA TTTGCTTTAT AAGTGAGGGT AGGGTGAGGG AGGACAGGCC AGTAGGGGGA   12720

GGGAAAGGGA GAGGGGAAGG GCAGGGGACT CAGGAAGCAG GGGGTCCCCA TCCCCAGCTG   12780

GGAAGAACAT GCTATCCAAT CTCATCTCTT GTAAATACAT GTCCCCCTGT GAGTTCTGGG   12840

CTGATTTGGG TCTCTCATAC CTCTGGGAAA CAGACCTTTT TCTCTCTTAC TGCTTCATGT   12900

AATTTTGTAT CACCTCTTCA CAATTTAGTT CGTACCTGGC TTGAAGCTGC TCACTGCTCA   12960

CACGCTGCCT CCTCAGCAGC CTCACTGCAT CTTTCTCTTC CCATGCAACA CCCTCTTCTA   13020

GTTACCACGG CAACCCCTGC AGCTCCTCTG CCTTTGTGCT CTGTTCCTGT CCAGCAGGGG   13080

TCTCCCAACA AGTGCTCTTT CCACCCCAAA GGGGCCTCTC CTTTTCTCCA CTGTCATAAT   13140

CTCTTTCCAT CTTACTTGCC CTTCTATACT TTCTCACATG TGGCTCCCCC TGAATTTTGC   13200

TTCCTTTGGG AGCTCATTCT TTTCGCCAAG GCTCACATGC TCCTTGCCTC TGCTCTGTGC   13260

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TGTGTACACA CGCTTTTCCC GTATGCTTTC TTCATGTTCA GTCACATGTG CTCTCGGGTG   13380

CCCTGCATTC ACAGCTACGT GTGCCCCTCT CATGGTCATG GGTCTGCCCT TGAGCGTGTT   13440

TGGGTAGGCA TGTGCAATTT GTCTAGCATG CTGAGTCATG TCTTTCCTAT TTGCACACGT   13500

CCATGTTTAT CCATGTACTT TCCCTGTGTA CCCTCCATGT ACCTTGTGTA CTTTCTTCCC   13560

TTAAATCATG GTATTCTTCT GACAGAGCCA TATGTACCCT ACCCTGCACA TTGTTATGCA   13620

CTTTTCCCCA ATTCATGTTT GGTGGGGCCA TCCACACCCT CTCCTTGTCA CAGAATCTCC   13680
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ATTTCTGCTC AGATTCCCCC CATCTCCATT GCATTCATGT ACTACCCTCA GTCTACACTC   13740

ACAATCATCT TCTCCCAAGA CTGCTCCCTT TTGTTTTGTG TTTTTTTGAG GGGAATTAAG   13800

GAAAAATAAG TGGGGGCAGG TTTGGAGAGC TGCTTCCAGT GGATAGTTGA TGAGAATCCT   13860

GACCAAAGGA AGGCACCCTT GACTGTTGGG ATAGACAGAT GGACCTATGG GGTGGGAGGT   13920

GGTGTCCCTT TCACACTGTG GTGTCTCTTG GGAAGGATC TCCCCGAATC TCAATAAACC   13980

AGTGAACAGT GTGACTCGGC ACCTTGCAGT CTTCCTGTGA ACAGAATGGG CTTCAATCCA   14040

AGAAGGGAGG CTCAGAGGAC TCCAAGTTCA TGAAAAGGCA TTAAAGCGGA GGGTGAAAAG   14100

AGGTGTTTTA TTGATCCATT GAGGGCTTAG CAGAATGAAG CAGGACATGA TTAAGTCTGA   14160

GATTAGTGAG TGAGGACACT ACTGGTTAAA AGTGTGGGCT CTGGAGTCAG ACTGCCAGGG   14220

TATCAGATCC AACCACATGC AAACATTTTC TTAGTCTCTA TTCCCCATGT CCTCATTTAT   14280

GAAAATGAGA ATAACAGTAA TACATTCCTC CATAGGTTGG GTACAAAGAC TATTATAAAT   14340

TGTGCATTCA GGTGCCTAGG TTGGCCCTTG GGCCATGGTA TATGTTGCGT GAATGTTAGC   14400

CTCTGTCCCT GCTGTTTAAT GAGTTCCTTG ACAGTAGTGG GCATGTATTG GGAGCCTGGA   14460

GCAAGTGCCT AAGCATCCCC TCTAGGGACG CTCCTTCCCA GGAACTAAGA AGAGTAAAAG   14520

AATGATGACT GCTAGAAGGT AATGGATGAG ATGGCTGCTG AGTGCTTCCA ACCTTAAACA   14580

TCTTTGTTTA GGAACTCTGA GCATCTTGGA AATAATTTGC TATCAAACTG AAAAAAAATC   14640

TTGAATGGAC AAGGGCAAAA ACATTTGCCT GAGACTTTAA ACATTTTTTG TGTCATCTTG   14700

GAGAGTGCTT TTTTGAAGCT CAAATTTTCT TTTATTTTGG CACTGATTTT TAAAGTGATT   14760

CTCAGATTTT TGTAAGACAG CTGCAAGGGT TGGATGGGCC CTGTCATTCA CTGACCTGTT   14820

AAGAGCCAAT TTCTGAACTT CCACTAAAGC ATGGGCTGGT TGAATCTTAG ACCAGTACTT   14880

GAAAAACTTT CCACTGTGAT TATCCACCTT GGACCAGTTG GACTTAATTT GAGTCTCTCT   14940

TCTTCCCACA GTGAAATATC CGCTAGGAAA AGAGAAGAAG TCTATGGAGT AGATAAGCCT   15000

SUBSTITUTE SHEET (RULE 26)

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GCAGTTTGGA AAATGAATAG TTGGCATCAG AACAGCAGCA GGAGGCTGGG TGTGGTGGCT   15060

CACGCCTGTA ATCCCAGCAC TTTGGGAGGC TGAGGTGGGT GGATCACGAG GTCAGGAGTT   15120

CAAGACCAGC CTGGCCAAGA TGGCGAAACC CTGTCTCTAC TAAAAATACA AAAATTAGCT   15180

GGGCGTGATG GTGGGTGCCT GTAATCTCAG CTACTCGGGA GGCTGAGGCA GATAATTGCT   15240

TGAACCCAGG AGATGAAGGT TGCAGTGAGT TTGTGCCACT GCACTCCAGC CTGGGCGACA   15300

GAGTGAGACT GTCTCAAAAA AAAAAAAAA GAAAAAAAA AAAGAAACAA CAGTAGCAGG     15360

AGCTATAGAA CAGCCCTGGG TAGAACCTAA AAGACCCAAA TTATCATCTC AAACTTGCAT   15420

TGCACTTAAG TGGGCTGTAA ATTATAAACA AAGGGTGAAA AGTTCTACTG TGGCCAAAGG   15480

TAAGCCAGAC ACTCTGCTAG CAGGAGTGCA GGAGTCGAGA GCCAAACGGT GCGGCTAGCA   15540

GAGTGCCCAG TGCAAAGGGG TGGGAAGGAG TGAGATTGAG AATATTAAAA AGGTACTTAG   15600

AAGAGAACTT GTAAGATTTT TACTGGCCAA ATTTAAAACA TGACTGAGCA CTATTTTTCA   15660

TACAGGCCTC CTACTAATAA GAAAACAATT TTGAGATAAC TACTTATTTG AGTTCACAGT   15720

TAATGTTCCT GATGATTAAG ATCAGTTGCA AATGTTCATC TGTCAATGCT TATCTACAAT   15780

GAGACTTCAT GTATTCATTT CTGAAAGTGT CTTTTCAGGG TGAATGGTGC TATTGATTAG   15840

CACTAATACT AATTATTAGT ACATTATATA TAATTACAAT GAGATATACA CACACATACA   15900

CACACACATA TATACATATA CACACACACA ATGATATATA ATTAATATAT AATTGTACCC   15960

CAAGGGGTGC AAAGGAGATG TGTTGCCAGG TGGAGAGGCT ACCGCTTGGC AGTTCTGGGA   16020

GGACTTGCTC CCTGTGCACT GTGAGGCAGG CTTTGCCTTT CAGACCTGCC TTTGGGTAGG   16080

GTTCAGATCA CTTTCTAACT CTGGAATGTC CTAGAATGTA GACTGCCTGC AGGCTTCCAT   16140

GTCCCCTGCT TTTCCCTGAC TTAGCCTGTT GCCTCCCTGC CTCCTGTTG GTTGTCTACC    16200

AGTAGAGAGC ACTTTGTGTG CACTTGGCTG CTACATTAGT TAGGTGATCT TCAACAAGTG   16260
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SUBSTITUTE SHEET (RULE 26)

TTGATGGTGA GTTGCTGTGG CAGGTGCTTT TTTTGGCACT GAGGCAAAAT GGTGAGTAAG   16320

ATGGCTTTCA AGCGTTGTAC CTTCTCGACG TGGGAAGATG ACCAGTAAGC AGAAAAACAA   16380

ACGAGATCAC TTAAGAGAGC AACCAGGAGT GTTGGGCATC TCACAGCCAT TAGCTCTGGT   16440

GTGAAGGACA AATCTAAAAG CAAGGGGACT GTGTGTTCAT TTTCTGGGGT CACAAAACTA   16500

AGGAGCAAAG CCAGTATTCA AACTGCATAT ATTATTATCT ATTGCCACAA AACCTGTTAC   16560

CCTAAATGGC TTCAGACAAC AATAATCATT TATTATCCAT CATGGTTTTT GTGGGCTAGA   16620

AATTCAGATA GGGTACAGTG GGGAGGGTTC ACCCTGCTCC ACAGCATCTG GAAGATCTGA   16680

AGTCTGAGGG TTGTTGTCCA AAAGATC   16707

(2) INFORMATION FOR SEQ ID NO: 62:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 50 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 62:

ATGCGCGCCG GCAGCCAACA TGCTGCTGCT GCTGCTGGTG CCTCTCTTCC   50

    (2) INFORMATION FOR SEQ ID NO: 63:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 25 base pairs
            (B) TYPE: nucleic acid
            (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 63:

GGTCATCCAG CGTTGAGGTG AAGAC   25

(2) INFORMATION FOR SEQ ID NO: 64:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 25 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 64:

GAAGGTTGCC AGATTATACA TCCGC   25

(2) INFORMATION FOR SEQ ID NO: 65:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 25 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 65:

CCACGATGAT TCGAGCATCT TGACG   25

(2) INFORMATION FOR SEQ ID NO: 66:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 18 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 66:

CTGGTTCCTC CCAATGTG   18

(2) INFORMATION FOR SEQ ID NO: 67:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 21 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 67:

CCAGTGGACT ATGAGATTGA G   21

(2) INFORMATION FOR SEQ ID NO: 68:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 18 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 68:

CTGGTTCCTC CCAATGTG   18

(2) INFORMATION FOR SEQ ID NO: 69:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 21 base pairs
        (B) TYPE: nucleic acid

                    (C) STRANDEDNESS: single
                    (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: DNA

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 69:

CCAGTGGACT ATGAGATTGA G   21

(2) INFORMATION FOR SEQ ID NO: 70:

            (i) SEQUENCE CHARACTERISTICS:
                    (A) LENGTH: 2700 base pairs
                    (B) TYPE: nucleic acid
                    (C) STRANDEDNESS: single
                    (D) TOPOLOGY: linear

            (ii) MOLECULE TYPE: cDNA to mRNA

            (iii) HYPOTHETICAL: NO

            (iv) ANTI-SENSE: NO

            (vi) ORIGINAL SOURCE:
                    (A) ORGANISM: Homo sapiens

            (ix) FEATURE:
                    (A) NAME/KEY: CDS
                    (B) LOCATION:1..2700

            (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 70:

ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC   48
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1   5   10   15

GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC   96
Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
         20   25   30

ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG   144
Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg

    35   40   45

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     GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG      192
     Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
 5        50              55              60

     TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG      240
     Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
          65              70              75              80
10
     TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT      288
     Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                    85              90              95

15   GTG AAT CGA ACG CCA CAC TCA GAA CGG CGC GCA GTG TAC ATC GGG GCA      336
     Val Asn Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala
                    100             105             110

     CTG TTT CCC ATG AGC GGG GGC TGG CCA GGG GGC CAG GCC TGC CAG CCC      384
20   Leu Phe Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro
               115             120             125

     GCG GTG GAG ATG GCG CTG GAG GAC GTG AAT AGC CGC AGG GAC ATC CTG      432
     Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu
25        130             135             140

     CCG GAC TAT GAG CTC AAG CTC ATC CAC CAC GAC AGC AAG TGT GAT CCA      480
     Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro
     145             150             155             160
30
     GGC CAA GCC ACC AAG TAC CTA TAT GAG CTG CTC TAC AAC GAC CCT ATC      528
     Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile
                    165             170             175

35   AAG ATC ATC CTT ATG CCT GGC TGC AGC TCT GTC TCC ACG CTG GTG GCT      576
     Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala
                    180             185             190

     GAG GCT GCT AGG ATG TGG AAC CTC ATT GTG CTT TCC TAT GGC TCC AGC      624
40   Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser  ʊ
                    195             200             205

     TCA CCA GCC CTG TCA AAC CGG CAG CGT TTC CCC ACT TTC TTC CGA ACG      672
```

SUBSTITUTE SHEET (RULE 26)

```
      Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr        —
          210             215             220


      CAC CCA TCA GCC ACA CTC CAC AAC CCT ACC CGC GTG AAA CTC TTT GAA        720
  5   His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu
          225             230             235             240


      AAG TGG GGC TGG AAG AAG ATT GCT ACC ATC CAG CAG ACC ACT GAG GTC        768
      Lys Trp Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val
  10                      245             250             255


      TTC ACT TCG ACT CTG GAC GAC CTG GAG GAA CGA GTG AAG GAG GCT GGA        816
      Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly
                      260             265             270
  15

      ATT GAG ATT ACT TTC CGC CAG AGT TTC TTC TCA GAT CCA GCT GTG CCC        864
      Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro
                  275             280             285


  20  GTC AAA AAC CTG AAG CGC CAG GAT GCC CGA ATC ATC GTG GGA CTT TTC        912
      Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe
                  290             295             300


      TAT GAG ACT GAA GCC CGG AAA GTT TTT TGT GAG GTG TAC AAG GAG CGT        960
  25  Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg
          305             310             315             320


      CTC TTT GGG AAG AAG TAC GTC TGG TTC CTC ATT GGG TGG TAT GCT GAC       1008
      Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp
  30                      325             330             335


      AAT TGG TTC AAG ATC TAC GAC CCT TCT ATC AAC TGC ACA GTG GAT GAG       1056
      Asn Trp Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu
                      340             345             350
  35

      ATG ACT GAG GCG GTG GAG GGC CAC ATC ACA ACT GAG ATT GTC ATG CTG       1104
      Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu
                  355             360             365


  40  AAT CCT GCC AAT ACC CGC AGC ATT TCC AAC ATG ACA TCC CAG GAA TTT       1152
      Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe
                  370             375             380
```

SUBSTITUTE SHEET (RULE 26)

```
GTG GAG AAA CTA ACC AAG CGA CTG AAA AGA CAC CCT GAG GAG ACA GGA          1200
Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly
385             390             395             400
```

```
GGC TTC CAG GAG GCA CCG CTG GCC TAT GAT GCC ATC TGG GCC TTG GCA          1248
Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala
            405             410             415
```

```
CTG GCC CTG AAC AAG ACA TCT GGA GGA GGC GGC CGT TCT GGT GTG CGC          1296
Leu Ala Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg
                420             425             430
```

```
CTG GAG GAC TTC AAC TAC AAC AAC CAG ACC ATT ACC GAC CAA ATC TAC          1344
Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr
            435             440             445
```

```
CGG GCA ATG AAC TCT TCG TCC TTT GAG GGT GTC TCT GGC CAT GTG GTG          1392
Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val
            450             455             460
```

```
TTT GAT GCC AGC GGC TCT CGG ATG GCA TGG ACG CTT ATC GAG CAG CTT          1440
Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu
465             470             475             480
```

```
CAG GGT GGC AGC TAC AAG AAG ATT GGC TAC TAT GAC AGC ACC AAG GAT          1488
Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp
            485             490             495
```

```
GAT CTT TCC TGG TCC AAA ACA GAT AAA TGG ATT GGA GGG TCC CCC CCA          1536
Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro
            500             505             510
```

```
GCT GAC CAG ACC CTG GTC ATC AAG ACA TTC CGC TTC CTG TCA CAG AAA          1584
Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys
            515             520             525
```

```
CTC TTT ATC TCC GTC TCA GTT CTC TCC AGC CTG GGC ATT GTC CTA GCT          1632
Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala
            530             535             540
```

```
GTT GTC TGT CTG TCC TTT AAC ATC TAC AAC TCA CAT GTC CGT TAT ATC          1680
Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile
545             550             555             560
```

```
     CAG AAC TCA CAG CCC AAC CTG AAC AAC CTG ACT GCT GTG GGC TGC TCA   .  1728
     Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser
                     565             570             575
 5
     CTG GCT TTA GCT GCT GTC TTC CCC CTG GGG CTC GAT GGT TAC CAC ATT      1776
     Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile
             580             585             590

10   GGG AGG AAC CAG TTT CCT TTC GTC TGC CAG GCC CGC CTC TGG CTC CTG      1824
     Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu
             595             600             605

     GGC CTG GGC TTT AGT CTG GGC TAC GGT TCC ATG TTC ACC AAG ATT TGG      1872
15   Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp
             610             615             620

     TGG GTC CAC ACG GTC TTC ACA AAG AAG GAA GAA AAG AAG GAG TGG AGG      1920
     Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg
20   625             630             635             640

     AAG ACT CTG GAA CCC TGG AAG CTG TAT GCC ACA GTG GGC CTG CTG GTG      1968
     Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val
                     645             650             655
25
     GGC ATG GAT GTC CTC ACT CTC GCC ATC TGG CAG ATC GTG GAC CCT CTG      2016
     Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu
                     660             665             670

30   CAC CGG ACC ATT GAG ACA TTT GCC AAG GAG GAA CCT AAG GAA GAT ATT      2064
     His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile
                 675             680             685

     GAC GTC TCT ATT CTG CCC CAG CTG GAG CAT TGC AGC TCC AGG AAG ATG      2112
35   Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met
             690             695             700

     AAT ACA TGG CTT GGC ATT TTC TAT GGT TAC AAG GGG CTG CTG CTG CTG      2160
     Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu
40   705             710             715             720

     CTG GGA ATC TTC CTT GCT TAT GAG ACC AAG AGT GTG TCC ACT GAG AAG      2208
     Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys
```

SUBSTITUTE SHEET (RULE 26)

```
                    725                    730                    735         —

        ATC AAT GAT CAC CGG GCT GTG GGC ATG GCT ATC TAC AAT GTG GCA GTC      2256
        Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val
  5             740                    745                    750

        CTG TGC CTC ATC ACT GCT CCT GTC ACC ATG ATT CTG TCC AGC CAG CAG      2304
        Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln
                755                    760                    765
 10
        GAT GCA GCC TTT GCC TTT GCC TCT CTT GCC ATA GTT TTC TCC TCC TAT      2352
        Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr
            770                    775                    780

 15     ATC ACT CTT GTT GTG CTC TTT GTG CCC AAG ATG CGC AGG CTG ATC ACC      2400
        Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr
        785                    790                    795                    800

        CGA GGG GAA TGG CAG TCG GAG GCG CAG GAC ACC ATG AAG ACA GGG TCA      2448
 20     Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly Ser
                        805                    810                    815

        TCG ACC AAC AAC AAC GAG GAG GAG AAG TCC CGG CTG TTG GAG AAG GAG      2496
        Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu
 25             820                    825                    830

        AAC CGT GAA CTG GAA AAG ATC ATT GCT GAG AAA GAG GAG CGT GTC TCT      2544
        Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser
                835                    840                    845
 30
        GAA CTG CGC CAT CAA CTC CAG TCT CGG CAG CAG CTC CGC TCC CGG CGC      2592
        Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg
            850                    855                    860

 35     CAC CCA CCG ACA CCC CCA GAA CCC TCT GGG GGC CTG CCC AGG GGA CCC      2640
        His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro Arg Gly Pro
        865                    870                    875                    880

        CCT GAG CCC CCC GAC CGG CTT AGC TGT GAT GGG AGT CGA GTG CAT TTG      2688
 40     Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu    υ
                        885                    890                    895

        CTT TAT AAG TGA                                                  ·   2700
        Leu Tyr Lys ***
```

SUBSTITUTE SHEET (RULE 26)

Leu Tyr Lys *

5   (2) INFORMATION FOR SEQ ID NO: 71:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 899 amino acids
            (B) TYPE: amino acid
10   (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 71:

15
    Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
        1   5   10   15

    Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
20   20   25   30

    Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
                35   40   45

25 Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
                50   55   60

    Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
        65   70   75   80
30
    Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                    85   90   95

    Val Asn Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala
35   100   105   110

    Leu Phe Pro Met Ser Gly Gly Trp Pro Gly Gly Gln Ala Cys Gln Pro
                115   120   125

40 Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg Asp Ile Leu   ᴜ
                130   135   140

    Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys Cys Asp Pro

    _____

145   150   155   160

Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile
                  165   170   175

Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala
                  180   185   190

Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser
         195   200   205

Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr
         210   215   220

His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu
225   230   235   240

Lys Trp Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val
                  245   250   255

Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly
                  260   265   270

Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro
         275   280   285

Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe
         290   295   300

Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg
305   310   315   320

Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp
                  325   330   335

Asn Trp Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu
                  340   345   350

Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu
         355   360   365

Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe
         370   375   380

SUBSTITUTE SHEET (RULE 26)

Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly
385   390   395   400

5 Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala
                   405   410   415

   Leu Ala Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg
                   420   425   430

10 Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr
                   435   440   445

   Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val
15   450   455   460

   Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu
   465   470   475   480

20 Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp
                   485   490   495

   Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro
                   500   505   510

25 Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys
                   515   520   525

   Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala
30   530   535   540

   Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile
   545   550   555   560

35 Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser
                   565   570   575

   Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile
                   580   585   590

40 Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu
                   595   600   605

SUBSTITUTE SHEET (RULE 26)

Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp
    610   615   620

Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg
625   630   635   640

Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val
              645   650   655

Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu
          660   665   670

His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile
          675   680   685

Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met
    690   695   700

Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu
705   710   715   720

Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys
              725   730   735

Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val
              740   745   750

Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln
    755   760   765

Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr
    770   775   780

Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr
785   790   795   800

Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly Ser
              805   810   815

Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu
          820   825   830

Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser

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H1865-1 WO SEQ   131

SUBSTITUTE SHEET (RULE 26)

```
              835                840                845
```

```
     Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg
         850                855                860
```

```
     His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro Arg Gly Pro
     865                870                875                880
```

```
     Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu
                        885                890                895
```

```
     Leu Tyr Lys
```

(2) INFORMATION FOR SEQ ID NO: 72:

   (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 2518 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

   (ii) MOLECULE TYPE: cDNA to mRNA

   (iii) HYPOTHETICAL: NO

   (vi) ORIGINAL SOURCE:
        (A) ORGANISM: Homo sapiens

   (ix) FEATURE:
        (A) NAME/KEY: CDS
        (B) LOCATION:1..294

   (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 72:

```
ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC        48
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
  1               5                  10                 15
```

```
GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC        96
Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
```

```
                20                    25                    30

ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG      144
Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
 5                  35                    40                    45

GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG      192
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
                    50                    55                    60
10
TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG      240
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
                65                    70                    75                    80

15 TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT   288
   Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                        85                    90                    95


GTG TGA TCCAGGCCAA GCCACCAAGT ACCTATATGA GCTGCTCTAC AACGACCCTA      344
20 Val  *


TCAAGATCAT CCTTATGCCT GGCTGCAGCT CTGTCTCCAC GCTGGTGGCT GAGGCTGCTA     404

25 GGATGTGGAA CCTCATTGTG CTTTCCTATG GCTCCAGCTC ACCAGCCCTG TCAAACCGGC   464

AGCGTTTCCC CACTTTCTTC CGAACGCACC CATCAGCCAC ACTCCACAAC CCTACCCGCG      524

TGAAACTCTT TGAAAAGTGG GGCTGGAAGA AGATTGCTAC CATCCAGCAG ACCACTGAGG      584
30
TCTTCACTTC GACTCTGGAC GACCTGGAGG AACGAGTGAA GGAGGCTGGA ATTGAGATTA      644

CTTTCCGCCA GAGTTTCTTC TCAGATCCAG CTGTGCCCGT CAAAAACCTG AAGCGCCAGG      704

35 ATGCCCGAAT CATCGTGGGA CTTTTCTATG AGACTGAAGC CCGGAAAGTT TTTTGTGAGG   764

TGTACAAGGA GCGTCTCTTT GGGAAGAAGT ACGTCTGGTT CCTCATTGGG TGGTATGCTG      824

ACAATTGGTT CAAGATCTAC GACCCTTCTA TCAACTGCAC AGTGGATGAG ATGACTGAGG      884
40
CGGTGGAGGG CCACATCACA ACTGAGATTG TCATGCTGAA TCCTGCCAAT ACCCGCAGCA      944

TTTCCAACAT GACATCCCAG GAATTTGTGG AGAAACTAAC CAAGCGACTG AAAAGACACC    1004
```

SUBSTITUTE SHEET (RULE 26)

CTGAGGAGAC AGGAGGCTTC CAGGAGGCAC CGCTGGCCTA TGATGCCATC TGGGCCTTGG   1064

CACTGGCCCT GAACAAGACA TCTGGAGGAG GCGGCCGTTC TGGTGTGCGC CTGGAGGACT   1124

TCAACTACAA CAACCAGACC ATTACCGACC AAATCTACCG GGCAATGAAC TCTTCGTCCT   1184

TTGAGGGTGT CTCTGGCCAT GTGGTGTTTG ATGCCAGCGG CTCTCGGATG GCATGGACGC   1244

TTATCGAGCA GCTTCAGGGT GGCAGCTACA AGAAGATTGG CTACTATGAC AGCACCAAGG   1304

ATGATCTTTC CTGGTCCAAA ACAGATAAAT GGATTGGAGG GTCCCCCCCA GCTGACCAGA   1364

CCCTGGTCAT CAAGACATTC CGCTTCCTGT CACAGAAACT CTTTATCTCC GTCTCAGTTC   1424

TCTCCAGCCT GGGCATTGTC CTAGCTGTTG TCTGTCTGTC CTTTAACATC TACAACTCAC   1484

ATGTCCGTTA TATCCAGAAC TCACAGCCCA ACCTGAACAA CCTGACTGCT GTGGGCTGCT   1544

CACTGGCTTT AGCTGCTGTC TTCCCCCTGG GGCTCGATGG TTACCACATT GGGAGGAACC   1604

AGTTTCCTTT CGTCTGCCAG GCCCGCCTCT GGCTCCTGGG CCTGGGCTTT AGTCTGGGCT   1664

ACGGTTCCAT GTTCACCAAG ATTTGGTGGG TCCACACGGT CTTCACAAAG AAGGAAGAAA   1724

AGAAGGAGTG GAGGAAGACT CTGGAACCCT GGAAGCTGTA TGCCACAGTG GGCCTGCTGG   1784

TGGGCATGGA TGTCCTCACT CTCGCCATCT GGCAGATCGT GGACCCTCTG CACCGGACCA   1844

TTGAGACATT TGCCAAGGAG GAACCTAAGG AAGATATTGA CGTCTCTATT CTGCCCCAGC   1904

TGGAGCATTG CAGCTCCAGG AAGATGAATA CATGGCTTGG CATTTTCTAT GGTTACAAGG   1964

GGCTGCTGCT GCTGCTGGGA ATCTTCCTTG CTTATGAGAC CAAGAGTGTG TCCACTGAGA   2024

AGATCAATGA TCACCGGGCT GTGGGCATGG CTATCTACAA TGTGGCAGTC CTGTGCCTCA   2084

TCACTGCTCC TGTCACCATG ATTCTGTCCA GCCAGCAGGA TGCAGCCTTT GCCTTTGCCT   2144

CTCTTGCCAT AGTTTTCTCC TCCTATATCA CTCTTGTTGT GCTCTTTGTG CCCAAGATGC   2204

GCAGGCTGAT CACCCGAGGG GAATGGCAGT CGGAGGCGCA GGACACCATG AAGACAGGGT   2264

SUBSTITUTE SHEET (RULE 26)

CATCGACCAA CAACAACGAG GAGGAGAAGT CCCGGCTGTT GGAGAAGGAG AACCGTGAAC   2324

TGGAAAAGAT CATTGCTGAG AAAGAGGAGC GTGTCTCTGA ACTGCGCCAT CAACTCCAGT   2384

CTCGGCAGCA GCTCCGCTCC CGGCGCCACC CACCGACACC CCCAGAACCC TCTGGGGGCC   2444

TGCCCAGGGG ACCCCCTGAG CCCCCCGACC GGCTTAGCTG TGATGGGAGT CGAGTGCATT   2504

TGCTTTATAA GTGA   2518

(2) INFORMATION FOR SEQ ID NO: 73:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 97 amino acids
            (B) TYPE: amino acid
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 73:

Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1   5   10   15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                20   25   30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35   40   45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
        50   55   60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65   70   75   80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                85   90   95

Val

(2) INFORMATION FOR SEQ ID NO: 74:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 2679 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA to mRNA

    (iii) HYPOTHETICAL: NO

    (iv) ANTI-SENSE: NO

    (vi) ORIGINAL SOURCE:
       (A) ORGANISM: Homo sapiens

    (ix) FEATURE:
       (A) NAME/KEY: CDS
       (B) LOCATION:1..2679

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 74:

```
ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC        48
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
1               5                  10                  15

GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC        96
Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                20                  25                  30

ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG       144
Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35                  40                  45

GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG       192
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
        50                  55                  60

TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG       240
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
    65                  70                  75                  80
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  TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT      288
  Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
              85                  90                  95
5
  GAA CGG CGC GCA GTG TAC ATC GGG GCA CTG TTT CCC ATG AGC GGG GGC      336
  Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
              100                 105                 110
10
  TGG CCA GGG GGC CAG GCC TGC CAG CCC GCG GTG GAG ATG GCG CTG GAG      384
  Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
              115                 120                 125

  GAC GTG AAT AGC CGC AGG GAC ATC CTG CCG GAC TAT GAG CTC AAG CTC      432
15 Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
              130                 135                 140

  ATC CAC CAC GAC AGC AAG TGT GAT CCA GGC CAA GCC ACC AAG TAC CTA      480
  Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
20 145                 150                 155                 160

  TAT GAG CTG CTC TAC AAC GAC CCT ATC AAG ATC ATC CTT ATG CCT GGC      528
  Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
              165                 170                 175
25
  TGC AGC TCT GTC TCC ACG CTG GTG GCT GAG GCT GCT AGG ATG TGG AAC      576
  Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
              180                 185                 190

30 CTC ATT GTG CTT TCC TAT GGC TCC AGC TCA CCA GCC CTG TCA AAC CGG      624
  Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
              195                 200                 205

  CAG CGT TTC CCC ACT TTC TTC CGA ACG CAC CCA TCA GCC ACA CTC CAC      672
35 Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
              210                 215                 220

  AAC CCT ACC CGC GTG AAA CTC TTT GAA AAG TGG GGC TGG AAG AAG ATT      720
  Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
40 225                 230                 235                 240

  GCT ACC ATC CAG CAG ACC ACT GAG GTC TTC ACT TCG ACT CTG GAC GAC      768
  Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
```

<pre>
                    245   250   255
</pre>

<pre>
   CTG GAG GAA CGA GTG AAG GAG GCT GGA ATT GAG ATT ACT TTC CGC CAG   816
   Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
5   260   265   270

   AGT TTC TTC TCA GAT CCA GCT GTG CCC GTC AAA AAC CTG AAG CGC CAG   864
   Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
          275   280   285
10
   GAT GCC CGA ATC ATC GTG GGA CTT TTC TAT GAG ACT GAA GCC CGG AAA   912
   Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
      290   295   300

15 GTT TTT TGT GAG GTG TAC AAG GAG CGT CTC TTT GGG AAG AAG TAC GTC   960
   Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
   305   310   315   320

   TGG TTC CTC ATT GGG TGG TAT GCT GAC AAT TGG TTC AAG ATC TAC GAC   1008
20 Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp
                  325   330   335

   CCT TCT ATC AAC TGC ACA GTG GAT GAG ATG ACT GAG GCG GTG GAG GGC   1056
   Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly
25   340   345   350

   CAC ATC ACA ACT GAG ATT GTC ATG CTG AAT CCT GCC AAT ACC CGC AGC   1104
   His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
          355   360   365
30
   ATT TCC AAC ATG ACA TCC CAG GAA TTT GTG GAG AAA CTA ACC AAG CGA   1152
   Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
          370   375   380

35 CTG AAA AGA CAC CCT GAG GAG ACA GGA GGC TTC CAG GAG GCA CCG CTG   1200
   Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
   385   390   395   400

   GCC TAT GAT GCC ATC TGG GCC TTG GCA CTG GCC CTG AAC AAG ACA TCT   1248
40 Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
                  405   410   415

   GGA GGA GGC GGC CGT TCT GGT GTG CGC CTG GAG GAC TTC AAC TAC AAC   1296
</pre>

SUBSTITUTE SHEET (RULE 26)

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        Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn        —
                    420             425             430

        AAC CAG ACC ATT ACC GAC CAA ATC TAC CGG GCA ATG AAC TCT TCG TCC      1344
   5    Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
                    435             440             445

        TTT GAG GGT GTC TCT GGC CAT GTG GTG TTT GAT GCC AGC GGC TCT CGG      1392
        Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
   10       450             455             460

        ATG GCA TGG ACG CTT ATC GAG CAG CTT CAG GGT GGC AGC TAC AAG AAG      1440
        Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
        465             470             475             480

   15   ATT GGC TAC TAT GAC AGC ACC AAG GAT GAT CTT TCC TGG TCC AAA ACA      1488
        Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                        485             490             495

   20   GAT AAA TGG ATT GGA GGG TCC CCC CCA GCT GAC CAG ACC CTG GTC ATC      1536
        Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile
                    500             505             510

        AAG ACA TTC CGC TTC CTG TCA CAG AAA CTC TTT ATC TCC GTC TCA GTT      1584
   25   Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile Ser Val Ser Val
                    515             520             525

        CTC TCC AGC CTG GGC ATT GTC CTA GCT GTT GTC TGT CTG TCC TTT AAC      1632
        Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn
   30       530             535             540

        ATC TAC AAC TCA CAT GTC CGT TAT ATC CAG AAC TCA CAG CCC AAC CTG      1680
        Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu
        545             550             555             560

   35   AAC AAC CTG ACT GCT GTG GGC TGC TCA CTG GCT TTA GCT GCT GTC TTC      1728
        Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu Ala Ala Val Phe
                        565             570             575

   40   CCC CTG GGG CTC GAT GGT TAC CAC ATT GGG AGG AAC CAG TTT CCT TTC      1776
        Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Asn Gln Phe Pro Phe
                    580             585             590
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SUBSTITUTE SHEET (RULE 26)

GTC TGC CAG GCC CGC CTC TGG CTC CTG GGC CTG GGC TTT AGT CTG GGC   1824
Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly
            595   600   605

5   TAC GGT TCC ATG TTC ACC AAG ATT TGG TGG GTC CAC ACG GTC TTC ACA   1872
Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His Thr Val Phe Thr
            610   615   620

     AAG AAG GAA GAA AAG AAG GAG TGG AGG AAG ACT CTG GAA CCC TGG AAG   1920
10 Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys
   625   630   635   640

     CTG TAT GCC ACA GTG GGC CTG CTG GTG GGC ATG GAT GTC CTC ACT CTC   1968
     Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp Val Leu Thr Leu
15   645   650   655

     GCC ATC TGG CAG ATC GTG GAC CCT CTG CAC CGG ACC ATT GAG ACA TTT   2016
     Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr Ile Glu Thr Phe
                 660   665   670
20

     GCC AAG GAG GAA CCT AAG GAA GAT ATT GAC GTC TCT ATT CTG CCC CAG   2064
     Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser Ile Leu Pro Gln
            675   680   685

25 CTG GAG CAT TGC AGC TCC AGG AAG ATG AAT ACA TGG CTT GGC ATT TTC   2112
     Leu Glu His Cys Ser Ser Arg Lys Met Asn Thr Trp Leu Gly Ile Phe
            690   695   700

     TAT GGT TAC AAG GGG CTG CTG CTG CTG CTG GGA ATC TTC CTT GCT TAT   2160
30 Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr
   705   710   715   720

     GAG ACC AAG AGT GTG TCC ACT GAG AAG ATC AAT GAT CAC CGG GCT GTG   2208
     Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp His Arg Ala Val
35   725   730   735

     GGC ATG GCT ATC TAC AAT GTG GCA GTC CTG TGC CTC ATC ACT GCT CCT   2256
     Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu Ile Thr Ala Pro
                 740   745   750
40

     GTC ACC ATG ATT CTG TCC AGC CAG CAG GAT GCA GCC TTT GCC TTT GCC   2304
     Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala
            755   760   765

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TCT CTT GCC ATA GTT TTC TCC TCC TAT ATC ACT CTT GTT GTG CTC TTT        2352
Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu Val Val Leu Phe
    770             775             780

GTG CCC AAG ATG CGC AGG CTG ATC ACC CGA GGG GAA TGG CAG TCG GAG        2400
Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu
785             790             795             800

GCG CAG GAC ACC ATG AAG ACA GGG TCA TCG ACC AAC AAC AAC GAG GAG        2448
Ala Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu
                805             810             815

GAG AAG TCC CGG CTG TTG GAG AAG GAG AAC CGT GAA CTG GAA AAG ATC        2496
Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile
            820             825             830

ATT GCT GAG AAA GAG GAG CGT GTC TCT GAA CTG CGC CAT CAA CTC CAG        2544
Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln
        835             840             845

TCT CGG CAG CAG CTC CGC TCC CGG CGC CAC CCA CCG ACA CCC CCA GAA        2592
Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu
        850             855             860

CCC TCT GGG GGC CTG CCC AGG GGA CCC CCT GAG CCC CCC GAC CGG CTT        2640
Pro Ser Gly Gly Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu
865             870             875             880

AGC TGT GAT GGG AGT CGA GTG CAT TTG CTT TAT AAG TGA                    2679
Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys  *
                885             890
```

(2) INFORMATION FOR SEQ ID NO: 75:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 892 amino acids
       (B) TYPE: amino acid
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 75:

```
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
1               5                   10                  15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
            20                  25                  30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
        35                  40                  45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
        50                  55                  60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
65                  70                  75                  80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
            85                  90                  95

Glu Arg Arg Ala Val Tyr Ile Gly Ala Leu Phe Pro Met Ser Gly Gly
            100                 105                 110

Trp Pro Gly Gly Gln Ala Cys Gln Pro Ala Val Glu Met Ala Leu Glu
            115                 120                 125

Asp Val Asn Ser Arg Arg Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu
        130                 135                 140

Ile His His Asp Ser Lys Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu
145                 150                 155                 160

Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu Met Pro Gly
            165                 170                 175

Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg Met Trp Asn
            180                 185                 190

Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg
        195                 200                 205

Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala Thr Leu His
        210                 215                 220
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SUBSTITUTE SHEET (RULE 26)

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     Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile
     225             230             235             240

  5  Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr Leu Asp Asp
                 245             250             255

     Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln
                 260             265             270
10
     Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu Lys Arg Gln
                 275             280             285

     Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys
15       290             295             300

     Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val
     305             310             315             320

20   Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp
                 325             330             335

     Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala Val Glu Gly
                 340             345             350
25
     His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn Thr Arg Ser
                 355             360             365

     Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu Thr Lys Arg
30       370             375             380

     Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu
     385             390             395             400

35   Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser
                 405             410             415

     Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn
                 420             425             430
40
     Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser
                 435             440             445
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H1865-1 WO SEQ   143

```
       Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser Gly Ser Arg
           450             455             460

    5  Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys
           465             470             475             480

       Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr
                       485             490             495

   10  Asp Lys Trp Ile Gly Gly Ser Pro Pro Ala Asp Gln Thr Leu Val Ile
               500             505             510

       Lys Thr Phe Arg Phe Leu Ser Gln Lys Leu Phe Ile Ser Val Ser Val
               515             520             525

   15
       Leu Ser Ser Leu Gly Ile Val Leu Ala Val Val Cys Leu Ser Phe Asn
               530             535             540

       Ile Tyr Asn Ser His Val Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu
   20  545             550             555             560

       Asn Asn Leu Thr Ala Val Gly Cys Ser Leu Ala Leu Ala Ala Val Phe
                       565             570             575

   25  Pro Leu Gly Leu Asp Gly Tyr His Ile Gly Arg Asn Gln Phe Pro Phe
                       580             585             590

       Val Cys Gln Ala Arg Leu Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly
               595             600             605

   30
       Tyr Gly Ser Met Phe Thr Lys Ile Trp Trp Val His Thr Val Phe Thr
               610             615             620

       Lys Lys Glu Glu Lys Lys Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys
   35  625             630             635             640

       Leu Tyr Ala Thr Val Gly Leu Leu Val Gly Met Asp Val Leu Thr Leu
                       645             650             655

   40  Ala Ile Trp Gln Ile Val Asp Pro Leu His Arg Thr Ile Glu Thr Phe
                       660             665             670

       Ala Lys Glu Glu Pro Lys Glu Asp Ile Asp Val Ser Ile Leu Pro Gln
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SUBSTITUTE SHEET (RULE 26)

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              675                   680                   685

    Leu Glu His Cys Ser Ser Arg Lys Met Asn Thr Trp Leu Gly Ile Phe
        690                   695                   700

5   Tyr Gly Tyr Lys Gly Leu Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr
    705                   710                   715                   720

    Glu Thr Lys Ser Val Ser Thr Glu Lys Ile Asn Asp His Arg Ala Val
10                    725                   730                   735

    Gly Met Ala Ile Tyr Asn Val Ala Val Leu Cys Leu Ile Thr Ala Pro
                  740                   745                   750

15  Val Thr Met Ile Leu Ser Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala
                  755                   760                   765

    Ser Leu Ala Ile Val Phe Ser Ser Tyr Ile Thr Leu Val Val Leu Phe
        770                   775                   780

20  Val Pro Lys Met Arg Arg Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu
    785                   790                   795                   800

    Ala Gln Asp Thr Met Lys Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu
25                    805                   810                   815

    Glu Lys Ser Arg Leu Leu Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile
                  820                   825                   830

30  Ile Ala Glu Lys Glu Glu Arg Val Ser Glu Leu Arg His Gln Leu Gln
                  835                   840                   845

    Ser Arg Gln Gln Leu Arg Ser Arg Arg His Pro Pro Thr Pro Pro Glu
        850                   855                   860

35  Pro Ser Gly Gly Leu Pro Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu
    865                   870                   875                   880

    Ser Cys Asp Gly Ser Arg Val His Leu Leu Tyr Lys
40                    885                   890
```

(2) INFORMATION FOR SEQ ID NO: 76:

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        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 2661 base pairs
            (B) TYPE: nucleic acid
  5         (C) STRANDEDNESS: single
            (D) TOPOLOGY: linear


       (ii) MOLECULE TYPE: cDNA to mRNA


 10    (iii) HYPOTHETICAL: NO


        (iv) ANTI-SENSE: NO


        (vi) ORIGINAL SOURCE:
 15         (A) ORGANISM: Homo sapiens


        (ix) FEATURE:
            (A) NAME/KEY: CDS
            (B) LOCATION:1..2661
 20
        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 76:


       ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC        48
       Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 25    1               5                   10                  15


       GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC        96
       Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                       20                  25                  30
 30
       ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG       144
       Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
                   35                  40                  45


 35    GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG       192
       Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
               50                  55                  60


       TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG       240
 40    Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
       65                  70                  75                  80


       TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT       288
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     Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys        —
                      85              90                  95


     GTG AAT CGA ACG CCA CAC TCA GAA CGG CGC GCA GTG TAC ATC GGG GCA        336
   5 Val Asn Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala
                 100             105                 110


     CTG TTT CCC GCG GTG GAG ATG GCG CTG GAG GAC GTG AAT AGC CGC AGG        384
     Leu Phe Pro Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg
  10          115             120                 125


     GAC ATC CTG CCG GAC TAT GAG CTC AAG CTC ATC CAC CAC GAC AGC AAG        432
     Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys
          130             135                 140

  15
     TGT GAT CCA GGC CAA GCC ACC AAG TAC CTA TAT GAG CTG CTC TAC AAC        480
     Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn
     145             150                 155                 160


  20 GAC CCT ATC AAG ATC ATC CTT ATG CCT GGC TGC AGC TCT GTC TCC ACG        528
     Asp Pro Ile Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr
                 165                 170                 175


     CTG GTG GCT GAG GCT GCT AGG ATG TGG AAC CTC ATT GTG CTT TCC TAT        576
  25 Leu Val Ala Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr
                 180                 185                 190


     GGC TCC AGC TCA CCA GCC CTG TCA AAC CGG CAG CGT TTC CCC ACT TTC        624
     Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe
  30          195                 200                 205


     TTC CGA ACG CAC CCA TCA GCC ACA CTC CAC AAC CCT ACC CGC GTG AAA        672
     Phe Arg Thr His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys
          210             215                 220

  35
     CTC TTT GAA AAG TGG GGC TGG AAG AAG ATT GCT ACC ATC CAG CAG ACC        720
     Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr
     225             230                 235                 240


  40 ACT GAG GTC TTC ACT TCG ACT CTG GAC GAC CTG GAG GAA CGA GTG AAG        768
     Thr Glu Val Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys
                 245                 250                 255
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SUBSTITUTE SHEET (RULE 26)

GAG GCT GGA ATT GAG ATT ACT TTC CGC CAG AGT TTC TTC TCA GAT CCA   816
Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro
            260   265   270

5   GCT GTG CCC GTC AAA AAC CTG AAG CGC CAG GAT GCC CGA ATC ATC GTG   864
    Ala Val Pro Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val
                275   280   285

    GGA CTT TTC TAT GAG ACT GAA GCC CGG AAA GTT TTT TGT GAG GTG TAC   912
10 Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr
            290   295   300

    AAG GAG CGT CTC TTT GGG AAG AAG TAC GTC TGG TTC CTC ATT GGG TGG   960
    Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp
15 305   310   315   320

    TAT GCT GAC AAT TGG TTC AAG ATC TAC GAC CCT TCT ATC AAC TGC ACA   1008
    Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr
                325   330   335
20
    GTG GAT GAG ATG ACT GAG GCG GTG GAG GGC CAC ATC ACA ACT GAG ATT   1056
    Val Asp Glu Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile
                340   345   350

25 GTC ATG CTG AAT CCT GCC AAT ACC CGC AGC ATT TCC AAC ATG ACA TCC   1104
    Val Met Leu Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser
                355   360   365

    CAG GAA TTT GTG GAG AAA CTA ACC AAG CGA CTG AAA AGA CAC CCT GAG   1152
30 Gln Glu Phe Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu
            370   375   380

    GAG ACA GGA GGC TTC CAG GAG GCA CCG CTG GCC TAT GAT GCC ATC TGG   1200
    Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp
35 385   390   395   400

    GCC TTG GCA CTG GCC CTG AAC AAG ACA TCT GGA GGA GGC GGC CGT TCT   1248
    Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser
                405   410   415
40
    GGT GTG CGC CTG GAG GAC TTC AAC TAC AAC AAC CAG ACC ATT ACC GAC   1296
    Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp
                420   425   430

CAA ATC TAC CGG GCA ATG AAC TCT TCG TCC TTT GAG GGT GTC TCT GGC   1344
Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly
        435   440   445

CAT GTG GTG TTT GAT GCC AGC GGC TCT CGG ATG GCA TGG ACG CTT ATC   1392
His Val Val Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile
        450   455   .   460

GAG CAG CTT CAG GGT GGC AGC TAC AAG AAG ATT GGC TAC TAT GAC AGC   1440
Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser
465   470   475   480

ACC AAG GAT GAT CTT TCC TGG TCC AAA ACA GAT AAA TGG ATT GGA GGG   1488
Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly
                485   490   495

TCC CCC CCA GCT GAC CAG ACC CTG GTC ATC AAG ACA TTC CGC TTC CTG   1536
Ser Pro Pro Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu
                500   505   510

TCA CAG AAA CTC TTT ATC TCC GTC TCA GTT CTC TCC AGC CTG GGC ATT   1584
Ser Gln Lys Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile
        515   520   525

GTC CTA GCT GTT GTC TGT CTG TCC TTT AAC ATC TAC AAC TCA CAT GTC   1632
Val Leu Ala Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val
        530   535   540

CGT TAT ATC CAG AAC TCA CAG CCC AAC CTG AAC AAC CTG ACT GCT GTG   1680
Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val
545   550   555   560

GGC TGC TCA CTG GCT TTA GCT GCT GTC TTC CCC CTG GGG CTC GAT GGT   1728
Gly Cys Ser Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly
                565   .   570   575

TAC CAC ATT GGG AGG AAC CAG TTT CCT TTC GTC TGC CAG GCC CGC CTC   1776
Tyr His Ile Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu
                580   585   590

TGG CTC CTG GGC CTG GGC TTT AGT CTG GGC TAC GGT TCC ATG TTC ACC   1824
Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr

---

                595   600   605

```
AAG ATT TGG TGG GTC CAC ACG GTC TTC ACA AAG AAG GAA GAA AAG AAG      1872
Lys Ile Trp Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys
    610                 615                 620


GAG TGG AGG AAG ACT CTG GAA CCC TGG AAG CTG TAT GCC ACA GTG GGC      1920
Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly
625                 630                 635                 640


CTG CTG GTG GGC ATG GAT GTC CTC ACT CTC GCC ATC TGG CAG ATC GTG      1968
Leu Leu Val Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val
                645                 650                 655


GAC CCT CTG CAC CGG ACC ATT GAG ACA TTT GCC AAG GAG GAA CCT AAG      2016
Asp Pro Leu His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys
                660                 665                 670


GAA GAT ATT GAC GTC TCT ATT CTG CCC CAG CTG GAG CAT TGC AGC TCC      2064
Glu Asp Ile Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser
                675                 680                 685


AGG AAG ATG AAT ACA TGG CTT GGC ATT TTC TAT GGT TAC AAG GGG CTG      2112
Arg Lys Met Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu
    690                 695                 700


CTG CTG CTG CTG GGA ATC TTC CTT GCT TAT GAG ACC AAG AGT GTG TCC      2160
Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser
705                 710                 715                 720


ACT GAG AAG ATC AAT GAT CAC CGG GCT GTG GGC ATG GCT ATC TAC AAT      2208
Thr Glu Lys Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn
                725                 730                 735


GTG GCA GTC CTG TGC CTC ATC ACT GCT CCT GTC ACC ATG ATT CTG TCC      2256
Val Ala Val Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser
                740                 745                 750


AGC CAG CAG GAT GCA GCC TTT GCC TTT GCC TCT CTT GCC ATA GTT TTC      2304
Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe
                755                 760                 765


TCC TCC TAT ATC ACT CTT GTT GTG CTC TTT GTG CCC AAG ATG CGC AGG      2352
```

```
Ser Ser Tyr Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg         —
    770             775             780
```

```
CTG ATC ACC CGA GGG GAA TGG CAG TCG GAG GCG CAG GAC ACC ATG AAG        2400
Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys
785             790             795             800
```

```
ACA GGG TCA TCG ACC AAC AAC AAC GAG GAG GAG AAG TCC CGG CTG TTG        2448
Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu
            805             810             815
```

```
GAG AAG GAG AAC CGT GAA CTG GAA AAG ATC ATT GCT GAG AAA GAG GAG        2496
Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu
            820             825             830
```

```
CGT GTC TCT GAA CTG CGC CAT CAA CTC CAG TCT CGG CAG CAG CTC CGC        2544
Arg Val Ser Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg
        835             840             845
```

```
TCC CGG CGC CAC CCA CCG ACA CCC CCA GAA CCC TCT GGG GGC CTG CCC        2592
Ser Arg Arg His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro
        850             855             860
```

```
AGG GGA CCC CCT GAG CCC CCC GAC CGG CTT AGC TGT GAT GGG AGT CGA        2640
Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg
865             870             875             880
```

```
GTG CAT TTG CTT TAT AAG TGA                                            2661
Val His Leu Leu Tyr Lys  *
                885
```


(2) INFORMATION FOR SEQ ID NO: 77:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 886 amino acids
            (B) TYPE: amino acid
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 77:

SUBSTITUTE SHEET (RULE 26)

```
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1               5                   10                  15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                20                  25                  30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
                35                  40                  45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
                50                  55                  60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65                 70                  75                  80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                85                  90                  95

Val Asn Arg Thr Pro His Ser Glu Arg Arg Ala Val Tyr Ile Gly Ala
                100                 105                 110

Leu Phe Pro Ala Val Glu Met Ala Leu Glu Asp Val Asn Ser Arg Arg
                115                 120                 125

Asp Ile Leu Pro Asp Tyr Glu Leu Lys Leu Ile His His Asp Ser Lys
                130                 135                 140

Cys Asp Pro Gly Gln Ala Thr Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn
145                 150                 155                 160

Asp Pro Ile Lys Ile Ile Leu Met Pro Gly Cys Ser Ser Val Ser Thr
                165                 170                 175

Leu Val Ala Glu Ala Ala Arg Met Trp Asn Leu Ile Val Leu Ser Tyr
                180                 185                 190

Gly Ser Ser Ser Pro Ala Leu Ser Asn Arg Gln Arg Phe Pro Thr Phe
                195                 200                 205

Phe Arg Thr His Pro Ser Ala Thr Leu His Asn Pro Thr Arg Val Lys
210                 215                 220

Leu Phe Glu Lys Trp Gly Trp Lys Lys Ile Ala Thr Ile Gln Gln Thr
```

SUBSTITUTE SHEET (RULE 26)

225   230   235   240

Thr Glu Val Phe Thr Ser Thr Leu Asp Asp Leu Glu Glu Arg Val Lys
              245   250   255

5

Glu Ala Gly Ile Glu Ile Thr Phe Arg Gln Ser Phe Phe Ser Asp Pro
              260   265   270

Ala Val Pro Val Lys Asn Leu Lys Arg Gln Asp Ala Arg Ile Ile Val

10   275   280   285

Gly Leu Phe Tyr Glu Thr Glu Ala Arg Lys Val Phe Cys Glu Val Tyr
          290   295   300

15 Lys Glu Arg Leu Phe Gly Lys Lys Tyr Val Trp Phe Leu Ile Gly Trp
    305   310   315   320

Tyr Ala Asp Asn Trp Phe Lys Ile Tyr Asp Pro Ser Ile Asn Cys Thr
              325   330   335

20

Val Asp Glu Met Thr Glu Ala Val Glu Gly His Ile Thr Thr Glu Ile
              340   345   350

Val Met Leu Asn Pro Ala Asn Thr Arg Ser Ile Ser Asn Met Thr Ser

25   355   360   365

Gln Glu Phe Val Glu Lys Leu Thr Lys Arg Leu Lys Arg His Pro Glu
          370   375   380

30 Glu Thr Gly Gly Phe Gln Glu Ala Pro Leu Ala Tyr Asp Ala Ile Trp
    385   390   395   400

Ala Leu Ala Leu Ala Leu Asn Lys Thr Ser Gly Gly Gly Gly Arg Ser
              405   410   415

35

Gly Val Arg Leu Glu Asp Phe Asn Tyr Asn Asn Gln Thr Ile Thr Asp
              420   425   430

Gln Ile Tyr Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly

40   435   440   445

His Val Val Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile
          450   455   460

```
     Glu Gln Leu Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser
     465             470             475             480

 5   Thr Lys Asp Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly
                     485             490             495

     Ser Pro Pro Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu
                 500             505             510
10
     Ser Gln Lys Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile
             515             520             525

     Val Leu Ala Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val
15       530             535             540

     Arg Tyr Ile Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val
     545             550             555             560

20   Gly Cys Ser Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly
                 565             570             575

     Tyr His Ile Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu
             580             585             590
25
     Trp Leu Leu Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr
             595             600             605

     Lys Ile Trp Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys
30       610             615             620

     Glu Trp Arg Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly
     625             630             635             640

35   Leu Leu Val Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val
                 645             650             655

     Asp Pro Leu His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys
                 660             665             670
40
     Glu Asp Ile Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser
             675             680             685
```

SUBSTITUTE SHEET (RULE 26)

```
    Arg Lys Met Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu
        690                 695                 700

    Leu Leu Leu Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser
5   705                 710                 715                 720

    Thr Glu Lys Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn
                        725                 730                 735

10  Val Ala Val Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser
                    740                 745                 750

    Ser Gln Gln Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe
                755                 760                 765

15
    Ser Ser Tyr Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg
            770                 775                 780

    Leu Ile Thr Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys
20  785                 790                 795                 800

    Thr Gly Ser Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu
                    805                 810                 815

25  Glu Lys Glu Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu
                820                 825                 830

    Arg Val Ser Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg
            835                 840                 845

30
    Ser Arg Arg His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro
        850                 855                 860

    Arg Gly Pro Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg
35  865                 870                 875                 880

    Val His Leu Leu Tyr Lys
                885
```

40

(2) INFORMATION FOR SEQ ID NO: 78:

    (i) SEQUENCE CHARACTERISTICS:

       (A) LENGTH: 1692 base pairs

       (B) TYPE: nucleic acid

       (C) STRANDEDNESS: single

       (D) TOPOLOGY: linear

  (ii) MOLECULE TYPE: cDNA to mRNA

  (iii) HYPOTHETICAL: NO

  (vi) ORIGINAL SOURCE:

       (A) ORGANISM: Homo sapiens

  (ix) FEATURE:

       (A) NAME/KEY: CDS

       (B) LOCATION:1..1692

  (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 78:

```
ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC      48
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
  1               5                  10                  15

GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC      96
Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                20                  25                  30

ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG     144
Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35                  40                  45

GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG     192
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
        50                  55                  60

TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG     240
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
    65                  70                  75                  80

TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT     288
Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                85                  90                  95

GTC CGA ATC TGC TCC AAG TCT TAT TTG ACC ATT ACC GAC CAA ATC TAC     336
```

```
    Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Ile Thr Asp Gln Ile Tyr        —
                100                 105                 110

    CGG GCA ATG AAC TCT TCG TCC TTT GAG GGT GTC TCT GGC CAT GTG GTG        384
  5 Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val
                115                 120                 125

    TTT GAT GCC AGC GGC TCT CGG ATG GCA TGG ACG CTT ATC GAG CAG CTT        432
    Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu
 10         130                 135                 140

    CAG GGT GGC AGC TAC AAG AAG ATT GGC TAC TAT GAC AGC ACC AAG GAT        480
    Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp
    145                 150                 155                 160

 15
    GAT CTT TCC TGG TCC AAA ACA GAT AAA TGG ATT GGA GGG TCC CCC CCA        528
    Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro
                    165                 170                 175

 20 GCT GAC CAG ACC CTG GTC ATC AAG ACA TTC CGC TTC CTG TCA CAG AAA        576
    Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys
                180                 185                 190

    CTC TTT ATC TCC GTC TCA GTT CTC TCC AGC CTG GGC ATT GTC CTA GCT        624
 25 Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala
                195                 200                 205

    GTT GTC TGT CTG TCC TTT AAC ATC TAC AAC TCA CAT GTC CGT TAT ATC        672
    Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile
 30     210                 215                 220

    CAG AAC TCA CAG CCC AAC CTG AAC AAC CTG ACT GCT GTG GGC TGC TCA        720
    Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser
    225                 230                 235                 240

 35
    CTG GCT TTA GCT GCT GTC TTC CCC CTG GGG CTC GAT GGT TAC CAC ATT        768
    Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile
                    245                 250                 255

 40 GGG AGG AAC CAG TTT CCT TTC GTC TGC CAG GCC CGC CTC TGG CTC CTG        816
    Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu
                260                 265                 270
```

```
    GGC CTG GGC TTT AGT CTG GGC TAC GGT TCC ATG TTC ACC AAG ATT TGG        864
    Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp
            275                 280                 285

 5  TGG GTC CAC ACG GTC TTC ACA AAG AAG GAA GAA AAG AAG GAG TGG AGG        912
    Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg
            290                 295                 300

    AAG ACT CTG GAA CCC TGG AAG CTG TAT GCC ACA GTG GGC CTG CTG GTG        960
10  Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val
    305                 310                 315                 320

    GGC ATG GAT GTC CTC ACT CTC GCC ATC TGG CAG ATC GTG GAC CCT CTG       1008
    Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu
15                  325                 330                 335

    CAC CGG ACC ATT GAG ACA TTT GCC AAG GAG GAA CCT AAG GAA GAT ATT       1056
    His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile
                    340                 345                 350
20
    GAC GTC TCT ATT CTG CCC CAG CTG GAG CAT TGC AGC TCC AGG AAG ATG       1104
    Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met
                    355                 360                 365

25  AAT ACA TGG CTT GGC ATT TTC TAT GGT TAC AAG GGG CTG CTG CTG CTG       1152
    Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu
            370                 375                 380

    CTG GGA ATC TTC CTT GCT TAT GAG ACC AAG AGT GTG TCC ACT GAG AAG       1200
30  Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys
    385                 390                 395                 400

    ATC AAT GAT CAC CGG GCT GTG GGC ATG GCT ATC TAC AAT GTG GCA GTC       1248
    Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val
35                  405                 410                 415

    CTG TGC CTC ATC ACT GCT CCT GTC ACC ATG ATT CTG TCC AGC CAG CAG       1296
    Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln
                    420                 425                 430
40
    GAT GCA GCC TTT GCC TTT GCC TCT CTT GCC ATA GTT TTC TCC TCC TAT       1344
    Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr
                    435                 440                 445
```

```
ATC ACT CTT GTT GTG CTC TTT GTG CCC AAG ATG CGC AGG CTG ATC ACC    1392
Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr
    450                 455             460

CGA GGG GAA TGG CAG TCG GAG GCG CAG GAC ACC ATG AAG ACA GGG TCA    1440
Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly Ser
465                 470             475                 480

TCG ACC AAC AAC AAC GAG GAG GAG AAG TCC CGG CTG TTG GAG AAG GAG    1488
Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu
                485             490                 495

AAC CGT GAA CTG GAA AAG ATC ATT GCT GAG AAA GAG GAG CGT GTC TCT    1536
Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser
            500             505             510

GAA CTG CGC CAT CAA CTC CAG TCT CGG CAG CAG CTC CGC TCC CGG CGC    1584
Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg
        515             520             525

CAC CCA CCG ACA CCC CCA GAA CCC TCT GGG GGC CTG CCC AGG GGA CCC    1632
His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro Arg Gly Pro
    530             535             540

CCT GAG CCC CCC GAC CGG CTT AGC TGT GAT GGG AGT CGA GTG CAT TTG    1680
Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu
545             550             555                 560

CTT TAT AAG TGA                                                    1692
Leu Tyr Lys  *
```

(2) INFORMATION FOR SEQ ID NO: 79:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 563 amino acids
            (B) TYPE: amino acid
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 79:

```
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1               5               10              15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
            20              25              30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35              40              45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
            50              55              60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65              70              75              80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
            85              90              95

Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Ile Thr Asp Gln Ile Tyr
            100             105             110

Arg Ala Met Asn Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val
            115             120             125

Phe Asp Ala Ser Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu
            130             135             140

Gln Gly Gly Ser Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp
145             150             155             160

Asp Leu Ser Trp Ser Lys Thr Asp Lys Trp Ile Gly Gly Ser Pro Pro
            165             170             175

Ala Asp Gln Thr Leu Val Ile Lys Thr Phe Arg Phe Leu Ser Gln Lys
            180             185             190

Leu Phe Ile Ser Val Ser Val Leu Ser Ser Leu Gly Ile Val Leu Ala
            195             200             205

Val Val Cys Leu Ser Phe Asn Ile Tyr Asn Ser His Val Arg Tyr Ile
            210             215             220
```

SUBSTITUTE SHEET (RULE 26)

```
        Gln Asn Ser Gln Pro Asn Leu Asn Asn Leu Thr Ala Val Gly Cys Ser
        225             230             235             240

    5   Leu Ala Leu Ala Ala Val Phe Pro Leu Gly Leu Asp Gly Tyr His Ile
                    245             250             255

        Gly Arg Asn Gln Phe Pro Phe Val Cys Gln Ala Arg Leu Trp Leu Leu
                    260             265             270
   10
        Gly Leu Gly Phe Ser Leu Gly Tyr Gly Ser Met Phe Thr Lys Ile Trp
                    275             280             285

        Trp Val His Thr Val Phe Thr Lys Lys Glu Glu Lys Lys Glu Trp Arg
   15   290             295             300

        Lys Thr Leu Glu Pro Trp Lys Leu Tyr Ala Thr Val Gly Leu Leu Val
        305             310             315             320

   20   Gly Met Asp Val Leu Thr Leu Ala Ile Trp Gln Ile Val Asp Pro Leu
                    325             330             335

        His Arg Thr Ile Glu Thr Phe Ala Lys Glu Glu Pro Lys Glu Asp Ile
                    340             345             350
   25
        Asp Val Ser Ile Leu Pro Gln Leu Glu His Cys Ser Ser Arg Lys Met
                    355             360             365

        Asn Thr Trp Leu Gly Ile Phe Tyr Gly Tyr Lys Gly Leu Leu Leu Leu
   30   370             375             380

        Leu Gly Ile Phe Leu Ala Tyr Glu Thr Lys Ser Val Ser Thr Glu Lys
        385             390             395             400

   35   Ile Asn Asp His Arg Ala Val Gly Met Ala Ile Tyr Asn Val Ala Val
                    405             410             415

        Leu Cys Leu Ile Thr Ala Pro Val Thr Met Ile Leu Ser Ser Gln Gln
                    420             425             430
   40
        Asp Ala Ala Phe Ala Phe Ala Ser Leu Ala Ile Val Phe Ser Ser Tyr
                    435             440             445
```

SUBSTITUTE SHEET (RULE 26)

```
Ile Thr Leu Val Val Leu Phe Val Pro Lys Met Arg Arg Leu Ile Thr
    450                 455             460
```

```
Arg Gly Glu Trp Gln Ser Glu Ala Gln Asp Thr Met Lys Thr Gly Ser
    465             470             475             480
```

```
Ser Thr Asn Asn Asn Glu Glu Glu Lys Ser Arg Leu Leu Glu Lys Glu
                485             490             495
```

```
Asn Arg Glu Leu Glu Lys Ile Ile Ala Glu Lys Glu Glu Arg Val Ser
            500             505             510
```

```
Glu Leu Arg His Gln Leu Gln Ser Arg Gln Gln Leu Arg Ser Arg Arg
        515             520             525
```

```
His Pro Pro Thr Pro Pro Glu Pro Ser Gly Gly Leu Pro Arg Gly Pro
    530             535             540
```

```
Pro Glu Pro Pro Asp Arg Leu Ser Cys Asp Gly Ser Arg Val His Leu
545             550             555             560
```

```
Leu Tyr Lys
```

(2) INFORMATION FOR SEQ ID NO: 80:

    (i) SEQUENCE CHARACTERISTICS:
        (A) LENGTH: 2602 base pairs
        (B) TYPE: nucleic acid
        (C) STRANDEDNESS: single
        (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA to mRNA

    (iii) HYPOTHETICAL: NO

    (vi) ORIGINAL SOURCE:
        (A) ORGANISM: Homo sapiens

    (ix) FEATURE:
        (A) NAME/KEY: CDS
        (B) LOCATION:1..318

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 80:

```
     ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC        48
 5   Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
      1               5                   10                  15


     GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC        96
     Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
10                  20                  25                  30


     ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG       144
     Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
                 35                  40                  45
15
     GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAT       192
     Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Asp
          50                  55                  60


20   GAA TCG AAC GCC ACA CTC AGA ACG GCG CGC AGT GTA CAT CGG GGC ACT       240
     Glu Ser Asn Ala Thr Leu Arg Thr Ala Arg Ser Val His Arg Gly Thr
     65                  70                  75                  80


     GTT TCC CAT GAG CGG GGG CTG GCC AGG GGG CCA GGC CTG CCA GCC CGC       288
25   Val Ser His Glu Arg Gly Leu Ala Arg Gly Pro Gly Leu Pro Ala Arg
                     85                  90                  95


     GGT GGA GAT GGC GCT GGA GGA CGT GAA TAG CCGCAGGGAC ATCCTGCCGG         338
     Gly Gly Asp Gly Ala Gly Gly Arg Glu  *
30                   100                 105


     ACTATGAGCT CAAGCTCATC CACCACGACA GCAAGTGTGA TCCAGGCCAA GCCACCAAGT     398

     ACCTATATGA GCTGCTCTAC AACGACCCTA TCAAGATCAT CCTTATGCCT GGCTGCAGCT     458
35
     CTGTCTCCAC GCTGGTGGCT GAGGCTGCTA GGATGTGGAA CCTCATTGTG CTTTCCTATG     518

     GCTCCAGCTC ACCAGCCCTG TCAAACCGGC AGCGTTTCCC CACTTTCTTC CGAACGCACC     578

40   CATCAGCCAC ACTCCACAAC CCTACCCGCG TGAAACTCTT TGAAAAGTGG GGCTGGAAGA     638

     AGATTGCTAC CATCCAGCAG ACCACTGAGG TCTTCACTTC GACTCTGGAC GACCTGGAGG     698
```

AACGAGTGAA GGAGGCTGGA ATTGAGATTA CTTTCCGCCA GAGTTTCTTC TCAGATCCAG   758

CTGTGCCCGT CAAAAACCTG AAGCGCCAGG ATGCCCGAAT CATCGTGGGA CTTTTCTATG   818

AGACTGAAGC CCGGAAAGTT TTTTGTGAGG TGTACAAGGA GCGTCTCTTT GGGAAGAAGT   878

ACGTCTGGTT CCTCATTGGG TGGTATGCTG ACAATTGGTT CAAGATCTAC GACCCTTCTA   938

TCAACTGCAC AGTGGATGAG ATGACTGAGG CGGTGGAGGG CCACATCACA ACTGAGATTG   998

TCATGCTGAA TCCTGCCAAT ACCCGCAGCA TTTCCAACAT GACATCCCAG GAATTTGTGG   1058

AGAAACTAAC CAAGCGACTG AAAAGACACC CTGAGGAGAC AGGAGGCTTC CAGGAGGCAC   1118

CGCTGGCCTA TGATGCCATC TGGGCCTTGG CACTGGCCCT GAACAAGACA TCTGGAGGAG   1178

GCGGCCGTTC TGGTGTGCGC CTGGAGGACT TCAACTACAA CAACCAGACC ATTACCGACC   1238

AAATCTACCG GGCAATGAAC TCTTCGTCCT TTGAGGGTGT CTCTGGCCAT GTGGTGTTTG   1298

ATGCCAGCGG CTCTCGGATG GCATGGACGC TTATCGAGCA GCTTCAGGGT GGCAGCTACA   1358

AGAAGATTGG CTACTATGAC AGCACCAAGG ATGATCTTTC CTGGTCCAAA ACAGATAAAT   1418

GGATTGGAGG GTCCCCCCCA GCTGACCAGA CCCTGGTCAT CAAGACATTC CGCTTCCTGT   1478

CACAGAAACT CTTTATCTCC GTCTCAGTTC TCTCCAGCCT GGGCATTGTC CTAGCTGTTG   1538

TCTGTCTGTC CTTTAACATC TACAACTCAC ATGTCCGTTA TATCCAGAAC TCACAGCCCA   1598

ACCTGAACAA CCTGACTGCT GTGGGCTGCT CACTGGCTTT AGCTGCTGTC TTCCCCCTGG   1658

GGCTCGATGG TTACCACATT GGGAGGAACC AGTTTCCTTT CGTCTGCCAG GCCCGCCTCT   1718

GGCTCCTGGG CCTGGGCTTT AGTCTGGGCT ACGGTTCCAT GTTCACCAAG ATTTGGTGGG   1778

TCCACACGGT CTTCACAAAG AAGGAAGAAA AGAAGGAGTG GAGGAAGACT CTGGAACCCT   1838

GGAAGCTGTA TGCCACAGTG GGCCTGCTGG TGGGCATGGA TGTCCTCACT CTCGCCATCT   1898

GGCAGATCGT GGACCCTCTG CACCGGACCA TTGAGACATT TGCCAAGGAG GAACCTAAGG   1958

AAGATATTGA CGTCTCTATT CTGCCCCAGC TGGAGCATTG CAGCTCCAGG AAGATGAATA   2018

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CATGGCTTGG CATTTTCTAT GGTTACAAGG GGCTGCTGCT GCTGCTGGGA ATCTTCCTTG   2078

CTTATGAGAC CAAGAGTGTG TCCACTGAGA AGATCAATGA TCACCGGGCT GTGGGCATGG   2138

CTATCTACAA TGTGGCAGTC CTGTGCCTCA TCACTGCTCC TGTCACCATG ATTCTGTCCA   2198

GCCAGCAGGA TGCAGCCTTT GCCTTTGCCT CTCTTGCCAT AGTTTTCTCC TCCTATATCA   2258

CTCTTGTTGT GCTCTTTGTG CCCAAGATGC GCAGGCTGAT CACCCGAGGG GAATGGCAGT   2318

CGGAGGCGCA GGACACCATG AAGACAGGGT CATCGACCAA CAACAACGAG GAGGAGAAGT   2378

CCCGGCTGTT GGAGAAGGAG AACCGTGAAC TGGAAAAGAT CATTGCTGAG AAAGAGGAGC   2438

GTGTCTCTGA ACTGCGCCAT CAACTCCAGT CTCGGCAGCA GCTCCGCTCC CGGCGCCACC   2498

CACCGACACC CCCAGAACCC TCTGGGGGCC TGCCCAGGGG ACCCCCTGAG CCCCCCGACC   2558

GGCTTAGCTG TGATGGGAGT CGAGTGCATT TGCTTTATAA GTGA   2602

(2) INFORMATION FOR SEQ ID NO: 81:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 105 amino acids
            (B) TYPE: amino acid
            (D) TOPOLOGY: linear

      (ii) MOLECULE TYPE: protein

      (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 81:

Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
1   5   10   15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
            20   25   30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35   40   45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Asp

                    50   55   60

          Glu Ser Asn Ala Thr Leu Arg Thr Ala Arg Ser Val His Arg Gly Thr
           65   70   75   80

          Val Ser His Glu Arg Gly Leu Ala Arg Gly Pro Gly Leu Pro Ala Arg
                              85   90   95

          Gly Gly Asp Gly Ala Gly Gly Arg Glu
                             100   105

          (2) INFORMATION FOR SEQ ID NO: 82:

              (i) SEQUENCE CHARACTERISTICS:
                  (A) LENGTH: 2367 base pairs
                  (B) TYPE: nucleic acid
                  (C) STRANDEDNESS: single
                  (D) TOPOLOGY: linear

             (ii) MOLECULE TYPE: cDNA to mRNA

            (iii) HYPOTHETICAL: NO

             (vi) ORIGINAL SOURCE:
                  (A) ORGANISM: Homo sapiens

             (ix) FEATURE:
                  (A) NAME/KEY: CDS
                  (B) LOCATION:1..294

             (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 82:

          ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC   48
          Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
           1   5   10   15

          GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC   96
          Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                              20   25   30

          ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG   144
          Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg

          ───
          H1865-1 WO SEQ   166

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               35                40                45
```

```
GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG    192
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
     50                55                60
```

```
TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG    240
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65                70                75                80
```

```
TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT    288
Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                 85                90                95
```

```
GTG TGA TCCAGGCCAA GCCACCAAGT ACCTATATGA GCTGCTCTAC AACGACCCTA    344
Val  *
```

```
TCAAGATCAT CCTTATGCCT GGCTGCAGCT CTGTCTCCAC GCTGGTGGCT GAGGCTGCTA    404
```

```
GGATGTGGAA CCTCATTGTG CTTTCCTATG CTCCAGCTC ACCAGCCCTG TCAAACCGGC    464
```

```
AGCGTTTCCC CACTTTCTTC CGAACGCACC CATCAGCCAC ACTCCACAAC CCTACCCGCG    524
```

```
TGAAACTCTT TGAAAAGTGG GGCTGGAAGA AGATTGCTAC CATCCAGCAG ACCACTGAGG    584
```

```
TCTTCACTTC GACTCTGGAC GACCTGGAGG AACGAGTGAA GGAGGCTGGA ATTGAGATTA    644
```

```
CTTTCCGCCA GAGTTTCTTC TCAGATCCAG CTGTGCCCGT CAAAAACCTG AAGCGCCAGG    704
```

```
ATGCCCGAAT CATCGTGGGA CTTTTCTATG AGACTGAAGC CCGGAAAGTT TTTTGTGAGG    764
```

```
TGTACAAGGA GCGTCTCTTT GGGAAGAAGT ACGTCTGGTT CCTCATTGGG TGGTATGCTG    824
```

```
ACAATTGGTT CAAGATCTAC GACCCTTCTA TCAACTGCAC AGTGGATGAG ATGACTGAGG    884
```

```
CGGTGGAGGG CCACATCACA ACTGAGATTG TCATGCTGAA TCCTGCCAAT ACCCGCAGCA    944
```

```
TTTCCAACAT GACATCCCAG GAATTTGTGG AGAAACTAAC CAAGCGACTG AAAAGACACC    1004
```

```
CTGAGGAGAC AGGAGGCTTC CAGGAGGCAC CGCTGGCCTA TGATGCCATC TGGGCCTTGG    1064
```

```
CACTGGCCCT GAACAAGACA TCTGGAGGAG GCGGCCGTTC TGGTGTGCGC CTGGAGGACT    1124
```

SUBSTITUTE SHEET (RULE 26)

```
TCAACTACAA CAACCAGACC ATTACCGACC AAATCTACCG GGCAATGAAC TCTTCGTCCT    1184

TTGAGGGTGT CTCTGGCCAT GTGGTGTTTG ATGCCAGCGG CTCTCGGATG GCATGGACGC    1244

TTATCGAGCA GCTTCAGGGT GGCAGCTACA AGAAGATTGG CTACTATGAC AGCACCAAGG    1304

ATGATCTTTC CTGGTCCAAA ACAGATAAAT GGATTGTTAT ATCCAGAACT CACAGCCCAA    1364

CCTGAACAAC CTGACTGCTG TGGGCTGCTC ACTGGCTTTA GCTGCTGTCT TCCCCCTGGG    1424

GCTCGATGGT TACCACATTG GGAGGAACCA GTTTCCTTTC GTCTGCCAGG CCCGCCTCTG    1484

GCTCCTGGGC CTGGGCTTTA GTCTGGGCTA CGGTTCCATG TTCACCAAGA TTTGGTGGGT    1544

CCACACGGTC TTCACAAAGA AGGAAGAAAA GAAGGAGTGG AGGAAGACTC TGGAACCCTG    1604

GAAGCTGTAT GCCACAGTGG GCCTGCTGGT GGGCATGGAT GTCCTCACTC TCGCCATCTG    1664

GCAGATCGTG GACCCTCTGC ACCGGACCAT TGAGACATTT GCCAAGGAGG AACCTAAGGA    1724

AGATATTGAC GTCTCTATTC TGCCCCAGCT GGAGCATTGC AGCTCCAGGA AGATGAATAC    1784

ATGGCTTGGC ATTTTCTATG GTTACAAGGG CTGCTGCTG CTGCTGGGAA TCTTCCTTGC     1844

TTATGAGACC AAGAGTGTGT CCACTGAGAA GATCAATGAT CACCGGGCTG TGGGCATGGC    1904

TATCTACAAT GTGGCAGTCC TGTGCCTCAT CACTGCTCCT GTCACCATGA TTCTGTCCAG    1964

CCAGCAGGAT GCAGCCTTTG CCTTTGCCTC TCTTGCCATA GTTTTCTCCT CCTATATCAC    2024

TCTTGTTGTG CTCTTTGTGC CCAAGATGCG CAGGCTGATC ACCCGAGGGG AATGGCAGTC    2084

GGAGGCGCAG GACACCATGA AGACAGGGTC ATCGACCAAC AACAACGAGG AGGAGAAGTC    2144

CCGGCTGTTG GAGAAGGAGA ACCGTGAACT GGAAAAGATC ATTGCTGAGA AGAGGAGCG     2204

TGTCTCTGAA CTGCGCCATC AACTCCAGTC TCGGCAGCAG CTCCGCTCCC GGCGCCACCC    2264

ACCGACACCC CCAGAACCCT CTGGGGGCCT GCCCAGGGGA CCCCCTGAGC CCCCCGACCG    2324

GCTTAGCTGT GATGGGAGTC GAGTGCATTT GCTTTATAAG TGA                      2367
```

(2) INFORMATION FOR SEQ ID NO: 83:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 97 amino acids
       (B) TYPE: amino acid
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein

    (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 83:

```
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1           5               10              15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
             20              25              30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
             35              40              45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
         50              55              60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65              70              75              80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
             85              90              95

Val
```

(2) INFORMATION FOR SEQ ID NO: 84:

    (i) SEQUENCE CHARACTERISTICS:
       (A) LENGTH: 2489 base pairs
       (B) TYPE: nucleic acid
       (C) STRANDEDNESS: single
       (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
     (A) ORGANISM: Homo sapiens

(ix) FEATURE:
     (A) NAME/KEY: CDS
     (B) LOCATION:1..1491

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 84:

```
ATG TTG CTG CTG CTG CTA CTG GCG CCA CTC TTC CTC CGC CCC CCG GGC        48
Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1               5                  10                  15

GCG GGC GGG GCG CAG ACC CCC AAC GCC ACC TCA GAA GGT TGC CAG ATC        96
Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
                20                  25                  30

ATA CAC CCG CCC TGG GAA GGG GGC ATC AGG TAC CGG GGC CTG ACT CGG       144
Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35                  40                  45

GAC CAG GTG AAG GCT ATC AAC TTC CTG CCA GTG GAC TAT GAG ATT GAG       192
Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
        50                  55                  60

TAT GTG TGC CGG GGG GAG CGC GAG GTG GTG GGG CCC AAG GTC CGC AAG       240
Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
 65                  70                  75                  80

TGC CTG GCC AAC GGC TCC TGG ACA GAT ATG GAC ACA CCC AGC CGC TGT       288
Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                85                  90                  95

GTC CGA ATC TGC TCC AAG TCT TAT TTG ACC CTG GAA AAT GGG AAG GTT       336
Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
                100                 105                 110

TTC CTG ACG GGT GGG GAC CTC CCA GCT CTG GAC GGA GCC CGG GTG GAT       384
```

```
            Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
                    115                 120                 125
```

```
            TTC CGG TGT GAC CCC GAC TTC CAT CTG TGT GAT CCA GGC CAA GCC ACC       432
        5   Phe Arg Cys Asp Pro Asp Phe His Leu Cys Asp Pro Gly Gln Ala Thr
                    130                 135                 140
```

```
            AAG TAC CTA TAT GAG CTG CTC TAC AAC GAC CCT ATC AAG ATC ATC CTT       480
            Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu
        10  145                 150                 155                 160
```

```
            ATG CCT GGC TGC AGC TCT GTC TCC ACG CTG GTG GCT GAG GCT GCT AGG       528
            Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg
                            165                 170                 175
        15
```

```
            ATG TGG AAC CTC ATT GTG CTT TCC TAT GGC TCC AGC TCA CCA GCC CTG       576
            Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu
                        180                 185                 190
```

```
        20  TCA AAC CGG CAG CGT TTC CCC ACT TTC TTC CGA ACG CAC CCA TCA GCC       624
            Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala
                        195                 200                 205
```

```
            ACA CTC CAC AAC CCT ACC CGC GTG AAA CTC TTT GAA AAG TGG GGC TGG       672
        25  Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp
                    210                 215                 220
```

```
            AAG AAG ATT GCT ACC ATC CAG CAG ACC ACT GAG GTC TTC ACT TCG ACT       720
            Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr
        30  225                 230                 235                 240
```

```
            CTG GAC GAC CTG GAG GAA CGA GTG AAG GAG GCT GGA ATT GAG ATT ACT       768
            Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr
                            245                 250                 255
        35
```

```
            TTC CGC CAG AGT TTC TTC TCA GAT CCA GCT GTG CCC GTC AAA AAC CTG       816
            Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu
                        260                 265                 270
```

```
        40  AAG CGC CAG GAT GCC CGA ATC ATC GTG GGA CTT TTC TAT GAG ACT GAA       864
            Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu
                        275                 280                 285
```

GCC CGG AAA GTT TTT TGT GAG GTG TAC AAG GAG CGT CTC TTT GGG AAG   912
Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys
        290   295   300

AAG TAC GTC TGG TTC CTC ATT GGG TGG TAT GCT GAC AAT TGG TTC AAG   960
Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys
305   310   315   320

ATC TAC GAC CCT TCT ATC AAC TGC ACA GTG GAT GAG ATG ACT GAG GCG   1008
Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala
            325   330   335

GTG GAG GGC CAC ATC ACA ACT GAG ATT GTC ATG CTG AAT CCT GCC AAT   1056
Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn
            340   345   350

ACC CGC AGC ATT TCC AAC ATG ACA TCC CAG GAA TTT GTG GAG AAA CTA   1104
Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu
            355   360   365

ACC AAG CGA CTG AAA AGA CAC CCT GAG GAG ACA GGA GGC TTC CAG GAG   1152
Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu
        370   375   380

GCA CCG CTG GCC TAT GAT GCC ATC TGG GCC TTG GCA CTG GCC CTG AAC   1200
Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn
385   390   395   400

AAG ACA TCT GGA GGA GGC GGC CGT TCT GGT GTG CGC CTG GAG GAC TTC   1248
Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe
            405   410   415

AAC TAC AAC AAC CAG ACC ATT ACC GAC CAA ATC TAC CGG GCA ATG AAC   1296
Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn
            420   425   430

TCT TCG TCC TTT GAG GGT GTC TCT GGC CAT GTG GTG TTT GAT GCC AGC   1344
Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser
            435   440   445

GGC TCT CGG ATG GCA TGG ACG CTT ATC GAG CAG CTT CAG GGT GGC AGC   1392
Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser
        450   455   460

```
TAC AAG AAG ATT GGC TAC TAT GAC AGC ACC AAG GAT GAT CTT TCC TGG        1440
Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp
465             470             475             480

TCC AAA ACA GAT AAA TGG ATT GTT ATA TCC AGA ACT CAC AGC CCA ACC        1488
Ser Lys Thr Asp Lys Trp Ile Val Ile Ser Arg Thr His Ser Pro Thr
                485             490             495

TGA ACAACCTGAC TGCTGTGGGC TGCTCACTGG CTTTAGCTGC TGTCTTCCCC            1541
 *


CTGGGGCTCG ATGGTTACCA CATTGGGAGG AACCAGTTTC CTTTCGTCTG CCAGGCCCGC     1601

CTCTGGCTCC TGGGCCTGGG CTTTAGTCTG GGCTACGGTT CCATGTTCAC CAAGATTTGG     1661

TGGGTCCACA CGGTCTTCAC AAAGAAGGAA GAAAAGAAGG AGTGGAGGAA GACTCTGGAA     1721

CCCTGGAAGC TGTATGCCAC AGTGGGCCTG CTGGTGGGCA TGGATGTCCT CACTCTCGCC     1781

ATCTGGCAGA TCGTGGACCC TCTGCACCGG ACCATTGAGA CATTTGCCAA GGAGGAACCT     1841

AAGGAAGATA TTGACGTCTC TATTCTGCCC CAGCTGGAGC ATTGCAGCTC CAGGAAGATG     1901

AATACATGGC TTGGCATTTT CTATGGTTAC AAGGGGCTGC TGCTGCTGCT GGGAATCTTC     1961

CTTGCTTATG AGACCAAGAG TGTGTCCACT GAGAAGATCA ATGATCACCG GGCTGTGGGC     2021

ATGGCTATCT ACAATGTGGC AGTCCTGTGC CTCATCACTG CTCCTGTCAC CATGATTCTG     2081

TCCAGCCAGC AGGATGCAGC CTTTGCCTTT GCCTCTCTTG CCATAGTTTT CTCCTCCTAT     2141

ATCACTCTTG TTGTGCTCTT TGTGCCCAAG ATGCGCAGGC TGATCACCCG AGGGGAATGG     2201

CAGTCGGAGG CGCAGGACAC CATGAAGACA GGGTCATCGA CCAACAACAA CGAGGAGGAG     2261

AAGTCCCGGC TGTTGGAGAA GGAGAACCGT GAACTGGAAA AGATCATTGC TGAGAAAGAG     2321

GAGCGTGTCT CTGAACTGCG CCATCAACTC CAGTCTCGGC AGCAGCTCCG CTCCCGGCGC     2381

CACCCACCGA CACCCCCAGA ACCCTCTGGG GGCCTGCCCA GGGGACCCCC TGAGCCCCCC     2441
```

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GACCGGCTTA GCTGTGATGG GAGTCGAGTG CATTTGCTTT ATAAGTGA   2489

(2) INFORMATION FOR SEQ ID NO: 85:

        (i) SEQUENCE CHARACTERISTICS:
            (A) LENGTH: 496 amino acids
            (B) TYPE: amino acid
            (D) TOPOLOGY: linear

        (ii) MOLECULE TYPE: protein

        (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 85:

Met Leu Leu Leu Leu Leu Leu Ala Pro Leu Phe Leu Arg Pro Pro Gly
 1   5   10   15

Ala Gly Gly Ala Gln Thr Pro Asn Ala Thr Ser Glu Gly Cys Gln Ile
            20   25   30

Ile His Pro Pro Trp Glu Gly Gly Ile Arg Tyr Arg Gly Leu Thr Arg
            35   40   45

Asp Gln Val Lys Ala Ile Asn Phe Leu Pro Val Asp Tyr Glu Ile Glu
        50   55   60

Tyr Val Cys Arg Gly Glu Arg Glu Val Val Gly Pro Lys Val Arg Lys
65   70   75   80

Cys Leu Ala Asn Gly Ser Trp Thr Asp Met Asp Thr Pro Ser Arg Cys
                85   90   95

Val Arg Ile Cys Ser Lys Ser Tyr Leu Thr Leu Glu Asn Gly Lys Val
            100   105   110

Phe Leu Thr Gly Gly Asp Leu Pro Ala Leu Asp Gly Ala Arg Val Asp
            115   120   125

Phe Arg Cys Asp Pro Asp Phe His Leu Cys Asp Pro Gly Gln Ala Thr
        130   135   140

Lys Tyr Leu Tyr Glu Leu Leu Tyr Asn Asp Pro Ile Lys Ile Ile Leu
145   150   155   160

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```
     Met Pro Gly Cys Ser Ser Val Ser Thr Leu Val Ala Glu Ala Ala Arg
                 165                 170                 175

5    Met Trp Asn Leu Ile Val Leu Ser Tyr Gly Ser Ser Ser Pro Ala Leu
                     180                 185                 190

     Ser Asn Arg Gln Arg Phe Pro Thr Phe Phe Arg Thr His Pro Ser Ala
                 195                 200                 205
10
     Thr Leu His Asn Pro Thr Arg Val Lys Leu Phe Glu Lys Trp Gly Trp
                 210                 215                 220

     Lys Lys Ile Ala Thr Ile Gln Gln Thr Thr Glu Val Phe Thr Ser Thr
15   225                 230                 235                 240

     Leu Asp Asp Leu Glu Glu Arg Val Lys Glu Ala Gly Ile Glu Ile Thr
                     245                 250                 255

20   Phe Arg Gln Ser Phe Phe Ser Asp Pro Ala Val Pro Val Lys Asn Leu
                 260                 265                 270

     Lys Arg Gln Asp Ala Arg Ile Ile Val Gly Leu Phe Tyr Glu Thr Glu
                 275                 280                 285
25
     Ala Arg Lys Val Phe Cys Glu Val Tyr Lys Glu Arg Leu Phe Gly Lys
                 290                 295                 300

     Lys Tyr Val Trp Phe Leu Ile Gly Trp Tyr Ala Asp Asn Trp Phe Lys
30   305                 310                 315                 320

     Ile Tyr Asp Pro Ser Ile Asn Cys Thr Val Asp Glu Met Thr Glu Ala
                 325                 330                 335

35   Val Glu Gly His Ile Thr Thr Glu Ile Val Met Leu Asn Pro Ala Asn
                 340                 345                 350

     Thr Arg Ser Ile Ser Asn Met Thr Ser Gln Glu Phe Val Glu Lys Leu
                 355                 360                 365
40
     Thr Lys Arg Leu Lys Arg His Pro Glu Glu Thr Gly Gly Phe Gln Glu
                 370                 375                 380
```

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```
    Ala Pro Leu Ala Tyr Asp Ala Ile Trp Ala Leu Ala Leu Ala Leu Asn
    385             390             395             400

    Lys Thr Ser Gly Gly Gly Gly Arg Ser Gly Val Arg Leu Glu Asp Phe
5                   405             410             415

    Asn Tyr Asn Asn Gln Thr Ile Thr Asp Gln Ile Tyr Arg Ala Met Asn
                420             425             430

10  Ser Ser Ser Phe Glu Gly Val Ser Gly His Val Val Phe Asp Ala Ser
                435             440             445

    Gly Ser Arg Met Ala Trp Thr Leu Ile Glu Gln Leu Gln Gly Gly Ser
        450             455             460
15
    Tyr Lys Lys Ile Gly Tyr Tyr Asp Ser Thr Lys Asp Asp Leu Ser Trp
    465             470             475             480

    Ser Lys Thr Asp Lys Trp Ile Val Ile Ser Arg Thr His Ser Pro Thr

20                  485             490             495
```

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A. CLASSIFICATION OF SUBJECT MATTER

IPC6: C07K 14/705
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EMBL Databas Genbank/DDBJ, accession no. Y11044, Grifa A. et al: "GABA (gamma-amino-butyric acid)neurotransmission: identification and fine mapping of human GABA-B receptor gene"; Biochem. Biophys. Res. Commun. 250:240-245(1998)	1-6,11-13, 16-26
X	Nature, Volume 386, March 1997, Klemens Kaupmann et al, "Expression cloning of GABAB receptors uncovers similarity to metabotropic glutamate receptors" page 239 - page 246	1-6,11-13, 16-26
X	WO 9746675 A1 (NOVARTIS AG), 11 December 1997 (11.12.97), page 50 - page 56, claim 4	1-6,11-13, 16-26

| X | Further documents are listed in the continuation of Box C. | | X | See patent family annex. |

Date of the actual completion of the international search	Date of mailing of the international search report
23 March 1999	2 6 -03- 1999
Name and mailing address of the ISA Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. + 46 8 666 02 86	Authorized officer Patrick Andersson Telephone No. + 46 8 782 25 00

Form PCT ISA 210 (second sheet) (July 1992)

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	Dialog Information Services, File 34, SciSearch, Dialog accession no. 07157158, Goei VL et al: "Human gamma-aminobutyric acid B receptor gene: Complementary DNA cloning, expression, chromosomal location, and genomic organization", Biological Psychiatry, 1998, V44, N8(OCT 15), p659-666	1-6,11-13, 16-26
A	Brain Research Bulletin, Volume 38, No 6, 1995, Robert J. Washabau et al, "GABA Receptros in the Dorsal Motor Nucleus of the Vagus Influence Feline Lower Esophageal Sphincter and Gastric Function" page 587 - page 594	1-6,11-13, 16-26

INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 98/01947

Box I   Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II   Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See next page

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest   ☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1992)

According to PCT rule 13.2, an international application shall relate to one invention only or a group of inventions linked by one or more of the same or corresponding "special technical features", i.e. features that define a contribution which each of the inventions makes over the prior art.

The claimed invention relates to a nucleic acid sequence encoding a GABAB-receptor from either human or canine origin. A possible special technical features could have been nucleotide sequence encoding a GABAB-receptor. However a nucleotide sequence encoding a human GABAB-receptor is known from Grifa A. et. al., see the search report. Thus, the present application is considered to contain the following independent inventions:

Invention 1, claims 3-4, and the parts of claims 1-2 and 16-26 relating to claims 3-4:A human GABAB-receptor 1a, and related items,

Invention 2, claims 5-6, and the parts of claims 1-2 and 16-26 relating to claims 5-6:A human GABAB-receptor 1b, and related items,

Invention 3, claims 7-8, and the parts of claims 1-2 and 16-26 relating to claims 7-8:A human GABAB-receptor 1c, and related items,

Invention 4, claims 9-10, and the parts of claims 1-2 and 16-26 relating to claims 9-10:A human GABAB-receptor 1d, and related items,

Invention 5, claims 12-13, and the parts of claims 1, 11 and 16-26 relating to claims 12-13:A canine GABAB-receptor 1a, and related items.

Invention 6, claims 14-15, and the parts of claims 1, 11 and 16-26 relating to claims 14-15:A canine GABAB-receptor 1c, and related items.

The search has been limited to inventions 1, 2 and 5.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9746675 A1	11/12/97	AU 2028497 A	05/01/98